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ABSTRACT

Presented is the text of the Congressional hearings examining the etiology of hyperactivity and methods of treatment for hyperactive children. Sections cover witness testimony; statements; and additional information consisting of 15 reports, articles, and publications on the topic of food additives and drug therapy. Included are communications to E. Kennedy and H. Hodgkinson. (IM)

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HYPERACTIVE CHILDREN. 1975

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JOINT HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

OF THE

COMMITTEE ON
LABOR AND PUBLIC WELFARE

AND THE

SUBCOMMITTEE ON
ADMINISTRATIVE PRACTICE AND PROCEDURE

OF THE

COMMITTEE ON THE JUDICIARY
UNITED STATES SENATE

NINETY-FOURTH CONGRESS

FIRST SESSION

ON

EXAMINATION INTO THE CAUSES OF HYPERACTIVE CHILDREN AND THE METHODS USED FOR TREATING THESE YOUNG CHILDREN

SEPTEMBER 11, 1975

Printed for the Use of the Committee on Labor and Public Welfare
and the Committee on the Judiciary

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HYPERACTIVE CHILDREN, 1975

THURSDAY, SEPTEMBER 11, 1975

U.S. Senate,
Subcommittee on Health of the
Committee on Labor and Public Welfare,
Subcommittee on Administrative Practice
and Procedure of the Committee on the Judiciary,
Washington, D.C.

The subcommittees met, pursuant to notice, at 10:05 a.m., in room 4232, Dirksen Senate Office Building, Senator Edward M. Kennedy (chairman of the subcommittees), presiding.

Staff members present: Leroy G. Goldman, professional staff member and Jay B. Cutler, minority counsel.

Present: Senators Kennedy and Beall.

Senator Kennedy. We will come to order.

There are approximately 5 million children that are considered to be hyperactive children in this country. There has been a great deal of concern and interest as to the best way and means of treating these young children.

It has been brought to the attention of the subcommittees in recent times about certain drugs that were being required to be administered to children in order for the children to go to school in a certain area of California.

It has been brought to our attention that experiments are being done by Ben Feingold, a doctor and a very distinguished one, who has concerned himself with this particular problem. This research has been brought to the attention not only of our Committee, but also to the attention of many concerned medical people and parents. Some enormously interesting, imaginative and compelling research has been done on an alternative to a drug program.

I think that this research deserves the kind of hearing that we can have this morning before this Committee. I am very hopeful that we work with Dr. Feingold to find out whether the kinds of initial positive and hopeful results that he has demonstrated in helping hundreds of thousands of parents all over this country who are very much concerned with this particular problem.

So, doctor, we very much welcome you before this committee.

I think many of us have known of your background and have come to respect the great contributions that you have made in the whole area of medical policy and research. We are very much looking forward to your testimony here today.

There is a great sense of hope in this committee room. We went through a period yesterday of very considerable anguish with certain policies that were in effect in this country and I think today we have got a great sense of hope about another aspect of the health area.

We look forward to your comments. We will ask you to proceed now in your own manner.

STATEMENT OF BEN F. FEINGOLD, M.D., CHIEF EMERITUS, DEPARTMENT OF ALLERGY, KAISER-PERMANENTE MEDICAL CENTER, SAN FRANCISCO, CALIF.

Dr. FEINGOLD. Thank you, Senator. I appreciate your very gracious comments. They are very helpful.

I consider it my good fortune and singular privilege to have the opportunity to discuss this important subject with so distinguished and influential a body as this committee which has the authority to initiate the procedures necessary for the early resolution of this crisis.

Hyperkinesis, which is synonymous with hyperactivity is not a precise clinical entity but rather an umbrella term encompassing a number of characteristics, for example, fidgetiness, running about, short attention span, low threshold for frustration leading to tantrums, sleeplessness, muscular incoordination, cognitive and perceptive difficulties. All of these deficits occur more frequently in boys than in girls, usually about 5 or 6 to one and in some samples as high as 9 to 1. Although these children usually have a high IQ, they fail scholastically.

All the deficits do not occur in every child, so that each individual has his own mosaic of characteristics. The pattern varies not only from child to child but for any given child the characteristics may change from day to day and at times even from hour to hour. Not every child with this syndrome is hyperactive.

Because of the great variability and liability of the pattern and also depending upon the orientation of the observer, whether an educator, psychologist, psychiatrist, or pediatrician, we encounter no less than 38 names in the literature to identify this syndrome. The most common after hyperkinesis is minimal brain dysfunction (MBD), a term which is used to cover many related conditions.

The term "hyperkinesis" is of comparatively recent origin, dating to 1957. However, the condition has always been with us.

There are descriptions in the medical literature as early as 400 B.C. which are quite similar to the clinical pattern currently labeled as hyperkinesis or MBD.

What is new is the tremendous rise in the prevalence of the condition which has reached epidemic proportions. It is interesting to note that a graph projected for the estimated incidence of H–LD over the past 10 years parallels the Standard & Poor's curves for the dollar value for soft drinks and synthetic flavors over the same period.

There are no precise figures for the incidence, but estimates range from a low of 5 percent of the grade school population to a high of 28 percent and at times even as high as 40 percent in some school districts. No socioeconomic group is exempt.

The magnitude of the problem can be appreciated with the knowledge that 10 million children in this country are considered deficient in their learning abilities. Of these, approximately 5 million or perhaps even 6 or 7 million are hyperkinetic, and of this number conservatively 2 million children are victims of the promiscuous practice of treatment with behavior modifying drugs, for example, the stimulants, amphetamine and Ritalin; tranquilizers like Stelazine and Mellaril; and the antidepressants, Elavil and Tofranil. And very frequently classes of medications are combined to complete the job of making a zombie of the child.

Senator Kennedy. Do you think these drugs are widely overused?

Dr. Feingold. I very definitely think so.

I have a clipping here, very significant, if I may digress from my statement.

Senator Kennedy. Yes.

Dr. Feingold. I have here a clipping that I got from the San Francisco Chronicle dated Tuesday, Sept. 9, 1975, this week and I read it on the plane coming here.

It says:

"Suit Charges Drug Forced On Students."

And it reads:

> A suit charging that Taft City School District officials forced children to take the psychoactive drug Ritalin, as a condition of attending school was filed in Kern County Superior Court yesterday on behalf of 17 elementary schoolchildren.
>
> The complaint filed by the Youth Law Center of San Francisco charges that school district employees told some parents they would have to consent to their children taking the drug or the children would be excluded from public school or placed in special classes.
>
> The suit contends that the school district's practices violated constitutional and statutory rights of parents to send their children to public schools and to determine medical treatment for them without outside interference.
>
> It also charged that the school district's staff physician sometimes issued prescriptions for Ritalin without physical examination of the children.
>
> Ritalin is prescribed for so-called hyperactive children to make them more manageable in the classroom.
>
> The lawsuit filed yesterday does not challenge the use of Ritalin under all circumstances, but it is aimed at halting the practice of "coercing parents to agree to administration of the drug as a condition of attending school."

That probably indicates the nature and scope of the problem.

Senator Kennedy. I understand that that article reported that schoolteachers are the ones who are making the decision about the need of the children to take that particular drug. This drug is given in order for the child to be able to continue in the classroom. That is the way I read that.

Dr. Feingold. That is quite correct. It is my impression.

Senator Kennedy. It is not a doctor who is doing the deciding. Irrespective of what perhaps you and I believe about the overutilization of those drugs among children, it is not even a doctor, but it is a school official who requires the parent to administer that drug to the child in order for the child to participate in the classroom.

Dr. Feingold. Quite right.

Senator Kennedy. The question about the teachers themselves making those decisions is very interesting. I think any of us who see children, who have children or who have a lot of nieces and nephews, know they are fidgety, anxious, and maybe bored in some of their classrooms. Now we have a situation—at least in this reported area—where a schoolteacher who has some children who might not be as interested, who may be a little bored with the classroom, can require the children to take a drug in order to stay in the classroom.

I am not sure that that is a very hopeful or helpful sign. Are you?

Dr. **Feingold**. No.

Senator, I think there is another aspect of the problem which you addressed yourself to, and that is the so-called crowding syndrome.

Senator **Kennedy**. Which syndrome?

Dr. **Feingold**. Crowding syndrome.

In experimental psychology when we see a group of rats confined to small quarters, they become hyperactive and aggressive. If we extrapolate that to a schoolroom we find that if we put 1 or 2 hyperactive or aggressive children in a classroom of 20 or 30 children, all the children become hyperactive and the teacher becomes hyperactive, too.

Senator **Kennedy**. Maybe the teacher ought to take that. [Laughter.]

But I think this is a serious problem. The example which you presented reflects a continuation of a certain kind of mentality in this matter.

You gave this as an illustration and as an example of what is taking place in one school district. I would be interested in your professional judgment about the general overutilization of drugs, which you consider to be in the area of 5-odd million. You talk about 10 million children with some learning disabilities, 5 million of whom might be considered to be hyperactive children.

Professionally, do you believe that there is an overuse of drugs for these particular children; and, if so, what do you think of the health implications?

Dr. **Feingold**. I do not think there is any doubt about the overuse. The child is not examined and the prescription is just written out again and the children have no recourse.

Monday when I left my office, well, I have two situations to illustrate this point. I had a mother call me frantically from southern California with a child 5 years of age receiving 60 milligrams of Ritalin for several years. She asked the physician to put the child on a diet and the psychiatrist recommended that the child be taken from the mother and put into a foster home to correct.

Now, a child 5 years of age on Ritalin for 3 years.

Now, a second child in the office, he is a 17-year-old boy, and on 100 milligrams of Mellaril for 7 years.

Without studying the problem, without evaluating, without recourse to other options, they immediately go ahead and put them on drugs.

Senator **Kennedy**. And then there is the cost and the effect on the parents——

Dr. **Feingold**. And what is the effect upon the child? We do not know what are the long-range effects upon the child.

Senator **Kennedy**. That is right.

Dr. **Feingold**. There are no really broad long-range studies. Not over a period of a year or two, but many years. We do not know.

Is it reasonable to have a child on drugs from 5 to 10 years without some adverse effects after that period?

We are raising a population that is accustomed to drugs. We are talking about the drug problem. Let us start right here.

Senator KENNEDY. Why do you think that is?

Dr. FEINGOLD. Why the drug problem?

Senator KENNEDY. Why do you think there is such a growth in the use of drugs?

Dr. FEINGOLD. I imagine there are many factors. I imagine in many instances they are desperate, do not know what to do, have no direct treatment. That is one thing. I think there has been great pressure of publicity, advertising, from the pharmaceutical firms. You see these large double-page ads with pictures of children before and after, and without studying indications the physicians are influenced by that. I cannot help but feel this is—that this advertising to the public, advertising to the profession, contributes in great measure to the overutilization of drugs.

I do not think there is any need for that.

Senator KENNEDY. This is an area we are terribly interested in and in which we have conducted rather extensive hearings.

We have some important legislation to try to address the issue of overutilization. I do not think there is any question in my own mind about the overutilization of drugs. The kinds of dangers that you pointed out must be looked at. There is the danger of adverse drug reaction and there are other health consequences which may occur over a considerable period of time.

Well, let us proceed.

Dr. FEINGOLD. We must also be cognizant of the growing trend among law officers, social workers, psychologists, psychiatrists, and educators to attribute to behavioral disturbances and learning disabilities in childhood the rising incidence of antisocial behavior, delinquency, and criminality among adolescents and adults.

Our interest in food additives goes back about 20 years to the time when our laboratories were involved in studying the behavior of small chemicals which in the language of immunology are called haptens. On the clinical side of our program we undertook to study the adverse reactions to drugs and the adverse reactions to food colors and flavors, both of which are low molecular weight compounds. On the surface it would seem that drugs and additives are unrelated, but it must be recognized that except for terminology there is no difference between a compound ingested as a drug and one ingested as a food additive. It is appalling to learn that in spite of this identity, not a single food additive has ever been subjected to the careful pharmacological investigations required of compounds licensed for use as medication.

Senator KENNEDY. Do you think they should be?

Dr. FEINGOLD. I think there should be, Senator. I think we are entering a new era now. Some of the statements I am making that they did not think FDA was in a position really to evaluate it, we are now in a new discipline of behavior toxicology and it is pointing out to us the adverse reactions of behavior attributable to the ingestion of drugs. That information was not available to any of the agencies and now it is available.

I think it is important to develop that aspect, behavior toxicology, to determine precisely, if we can, what are the roles of the various compounds that influence behavior. What is so insidious about this and what is so treacherous is that the damage is probably being done in utero. It does not manifest itself until later in life. It is not obvious at birth.

Senator KENNEDY. Where do you draw the line? Where are you going to draw the line as to what should be tested and what should not be tested?

Dr. FEINGOLD. I think everything should be tested. We have to evaluate on the basis of benefit and risk. There is no compound exempt.

Senator KENNEDY. How big a job is that?

Dr. FEINGOLD. A considerable job, a tremendous job because we have no information at all. I think we can approach the problem in this way. As I develop this, you will see I point out that colors and flavors about which I am zeroing in, are nonessential to our food supply, no nutritional value whatsoever. If we deleted them from our food supply nothing would be lost. Why run the risk of using something like this until we can determine whether or not they are deleterious? Why wait until the damage is done?

Now we have a new discipline.

Senator KENNEDY. I suppose some would say there is no inherent danger in preservatives and other kinds of food additives. And if there is nothing poisonous or dangerous in them, why would you put all the food manufacturing companies to additional cost, which is going to reflect itself in additional cost to the consumers? Why would you do various kinds of tests? And what real public health service would be provided?

Dr. FEINGOLD. I do not think that is true, Senator. I feel that everyone of these compounds, particularly a synthetic compound, is a potential danger; and until we can prove it is not a potential danger, then I think it should not be licensed.

On the other hand it must be evaluated on the basis of how essential it is to our food supply. If we find it has a true function in distribution of our food supply, preserving shelf life and all, it should be permitted.

But if it does not have—for instance, it was brought to my attention, why is it necessary for a preservative to maintain the shelf life for a 4- or 5-year period, when without the preservative shelf life would be a year? That is what we have to evaluate realistically.

Senator KENNEDY. That is not being done now?

Dr. FEINGOLD. I do not think it is; no. I do not think it has even started. We have a tremendous job in reevaluating everything.

As far as behavior, we know nothing about it, not a single one of these compounds has been studied.

Senator KENNEDY. You are convinced that in a number of these instances that these food additives are really potentially dangerous to health if taken over a long period of time?

Dr. FEINGOLD. Let me say this: These food additives, particularly colors and flavors which we have been observing over a period of about 15, almost 20 years, we know they affect practically every system of the body, depending upon predisposition of the individual.

Now, the adverse reaction affecting all systems of the body have been documented in literature. They are pretty well known. Behavior is a new one.

I do not think there is any doubt that these occur in a considerable number of individuals—what percentage of the population we do not know, because many segments of the profession are not aware that these chemicals cause adverse reactions: headaches, nasal trouble, asthma, skin involvement, joint involvement, gastrointestinal involvement. There is the allergy situation.

We must address ourselves to studies to determine what are we dealing with, what is happening here? This is another thing we have to do, and that is, what is the dosage response. How much can we really tolerate on the average.

In our discussion this morning we are only concerned with two of the 13 categories of food additives. These are the synthetic food colors and flavors.

I do not wish to imply that the remaining classes of additives do not cause adverse reactions. They do. Actually, any compound in existence whether natural or synthetic can induce an adverse reaction if the individual has the appropriate genetic profile, that is, predisposition. Since this is true, each compound or group of compounds must be evaluated on the basis of risk compared with benefit.

Of all the additives introduced into our food supply, the colors and flavors are the most common causes of adverse reactions which affect practically every system of the body. In addition, the colors and flavors have no nutritional function. They are used for their cosmetic effect. Accordingly, the risk outweighs the benefit. If these chemicals were omitted from our food supply, nothing would be lost.

Of all the adverse reactions induced by the food colors and flavors perhaps the most dramatic and the most critical are the behavioral disturbances.

I should like to share with you briefly the surprise and drama generated by the very first patient observed in our studies.

Our first patient with a behavioral disturbance attributed to artificial colors and flavors was an adult. She was a 40-year-old female.

The patient reported to the allergy department with involvement of the face and eyes by giant hives which were both uncomfortable and grotesque looking. Following study of the case, the condition was attributed to an ingestion of artificial colors and flavors.

Accordingly, she was managed with a diet eliminating these chemicals. The response was rapid and complete. Ten days following this response, a call from the chief of psychiatry of our medical center inquired about the management of this patient. The psychiatrist reported the patient had been in psychotherapy for 2 years because of her behavioral disturbances characterized by aggression and hostility to psychiatric treatment. She did respond to the diet. A further conference with the patient confirmed that the diet not only controlled her hives but also her behavior. Any infraction of the diet was followed immediately by a recurrence of the behavioral disturbance as well as the hives.

Senator KENNEDY. You mean on the diet she was fine and off the diet she was ill?

Dr. FEINGOLD. That is right. Behavior and hives both came back very quickly.

The staff was informed of this response. Very soon there were reports of children who responded as well as adults.

Since we are allergists, our initial patients reported with physical complaints, for example respiratory or skin involvement. No mention was made of a behavioral disturbance. However, after treating the physical complaint with a diet eliminating artificial colors, the patients often reported dramatic alterations in their behavioral pattern. This was particularly true of children whose parents frequently reported a marked improvement in the behavior pattern both at home and at school following dietary management.

Initially, we were skeptical and surprised that dietary management could so dramatically influence the behavioral pattern. However, after analyzing the problem, our amazement and skepticism were dispelled with the realization that food additives like drugs are low molecular weight compounds. There are drugs that stimulate, drugs that depress, and drugs that modify the behavior of individuals. In clinical practice it is not unusual to modify behavior with drugs. Actually, this is constantly attempted in the treatment of hyperkinesis and MBD. We reasoned that among the thousands of chemicals added to our food supply there must be some compounds that influence behavior.

To confirm our observations we arranged to get children whose primary complaint was hyperkinesis or MBD. Following management with a diet eliminating all artificial colors and flavors, we again observed the rapid and dramatic responses in about 50 percent of cases as reported by our earlier patients. Within a few weeks and sometimes within a few days a complete reversal of the behavioral pattern was observed. In some cases the problem dated back to early infancy. Children who had been receiving medication for their behavior could discontinue the drug almost immediately. A rapid improvement in scholastic achievement was noted. Very early in our experience we learned that any infraction of the diet, either deliberate or accidental, that is a candy bar, a stick of gum, a cake, a cookie or a soft drink induced a recurrence of the pattern within 2 to 4 hours and persisted for 24 hours to 4 days.

Senator KENNEDY. Do you mean you could see these sort of turn on and off?

Dr. FEINGOLD. Yes. Very interesting.

Senator KENNEDY. Do I understand from testimony here that you were able to take the children off drugs completely?

Dr. FEINGOLD. That is right. Immediately. As a matter of fact in the early days we tapered them off, we tapered off the dosage. Some were on 100 milligrams for 4–5–6 years and we tapered them off. But we soon found that it was better to stop the drug immediately when we put them on the diet. We found that when the diet becomes effective, it becomes operant and the drug seems to stimulate these children. Whether it is the drug or the dye on the drug, we do not know. These drugs are dyed, coated with dyes, so we stop them immediately. They may be hyperkinetic for a day or two. We discontinue the drug. That is one of the assets of this. We are removing the toxic chemicals, not adding. We are taking away all these drugs and we are trying to correct them.

A double blind crossover study funded by the National Institute of Education was directed by Dr. C. Keith Conners of the University of Pittsburgh. This study has demonstrated at a high level of statistical significance that dietary management controls hyperactivity.

Over the past several years I have personally managed several hundred of these children. In addition, I have received reports of favorable responses from parents, physicians, psychiatrists and psychologists representing practically all 50 States as well as reports from many countries including Canada, England, France, Sweden and Germany. A letter from a psychiatrist of the Ministry of Health of New South Wales, Australia has reported successes with dietary management of hyperkinetic children.

The percentage of successes to date ranges from a low of 30 percent to a high of about 70 percent, with an average of about 50 percent. With such a success rating we should anticipate helping several million children in this country alone.

From these reports and our own experiences we have broadened our understanding of the problem. We have learned that the younger the child, the more rapid the response. For example, infants during the first year of life with a history of constant crying, sleeplessness, fretfulness, restlessness, not wishing to be cuddled or held will show a dramatic response within 24 to 36 hours following discontinuance of pediatric vitamin drops, a rich source of artificial colors and flavors. These drops have actually become a way of life with most young infants in this country. The child between 3 and 5 years will usually respond to dietary management after 3 days, while the prepubescent child of 5 to about 10 years of age will manifest a response after 10 days to 2 weeks of dietary management. Occasionally, it may require 4 to 6 weeks for the diet to be effective, especially if the child has been treated with long-acting drugs, for example amphetamine Spansules.

Since the successes are fewer after puberty, the postpubescent child is a problem that deserves special attention. Several possible causes for failure must be considered. Do the chemicals ingested by the mother cause intrauterine damage? Does the persistent exposure to these chemicals over a period of many years cause irreversible neurological damage? Does the constant frustration of a child with a high IQ who cannot perform to his full potential result in withdrawal and a lowered self-esteem which leads to antisocial behavior, that is lying, and stealing and eventually to juvenile delinquency?

The dietary management of the hyperkinetic child resolves itself into two programs. First, the clinical application of the diet and second, improving our understanding of the problem through research.

The need for clinical application of the program is both critical and urgent. There are millions of hyperkinetic children who are disrupting their homes and their classrooms. They are failing scholastically and are in constant conflict with their peers. As a sequel, antisocial behavior develops, characterized by lying, stealing, and various degrees of violence which in many cases can lead to juvenile delinquency. Although the diet must be applied empirically at present, it still offers promise of a favorable response in approximately 50 percent of the troubled children. This means that we should anticipate correcting the problem for several million children in this country.

Fortunately, the diet is very liberal and nutritious.

Senator KENNEDY. What could you eat on the diet?

Dr. FEINGOLD. Anything, just so it has no colors or flavors—anything. There are no restrictions at all, nothing. They have cereals. They have milk.

Senator KENNEDY. Ice cream?

Dr. Feingold. Ice cream, pure ice cream.

Senator Kennedy. Cake?

Dr. Feingold. Cake, cookies, pastries.

Senator Kennedy. I wish I could get on that diet. [Laughter.]

Dr. Feingold. There are practically very few restrictions. All we are taking out is these chemicals and nothing else.

Senator Kennedy. You might gain a little weight on it.

Dr. Feingold. We can outline one to control that, too.

Instead of adding a compound or a drug, we eliminate the harmful chemicals and discontinue all medications. The risk is nil, and the potential benefits are great.

It is our judgment that successful dietary management cannot be mandated. It must be generated from the grassroots. Toward this objective we are promoting the establishment of associations of parents at the school or school district level. These voluntary organizations will permit parent interaction offering a vehicle for the exchange of experiences, menus, recipes, as well as provide information on permissible foods available in the local markets. Such an association is already functioning successfully in Bridgeton, N.J.

With the recognition that a single infraction can induce a return of symptoms within 2 to 4 hours, absolute compliance with the diet becomes obligatory. Strict compliance frequently becomes a problem due to inadequate disclosure of chemicals on the food package and also the frustration caused by the hours required for checking labels which are frequently illegible and not understandable. The absence of pediatric medications—this is important because there is not a pediatric medication on the market that is free of artificial flavors. If one of these children becomes sick, it becomes difficult to treat. Unless we resort to adult medication and regulate the dosage.

I repeat, the absence of pediatric medications free of artificial colors and flavors also complicates compliance.

Senator Kennedy. That is an interesting point. When there are symptoms, children are given medication and the medication itself can compound the symptoms?

Dr. Feingold. I have had a number of pediatricians say that when treating a child they put them on recommended dosage and the child goes wild. Now, recognizing this they can prescribe accordingly. This is a very serious problem.

To assist the consumer to expedite shopping we are advocating the adoption of a symbol or logo to appear on every package of food or beverage which does not contain artificial colors and flavors. The logo will place no restrictions upon the food processor beyond the regulations imposed by the FDA. The logo will offer the consumer a free choice between foods with and without the chemicals in question. In addition, the logo will permit the natural laws of the marketplace to operate—the basic philosophy of a free society.

Research must involve many disciplines. Studies in the field of genetics may explain the selection of the individuals who react adversely to chemicals and also the preponderance of boys over girls—perhaps the high IQ we encounter in the children.

Research can utilize the observations in the field of behavioral toxicology, a newly emerging discipline which has demonstrated that chemicals can induce intrauterine damage which is not apparent at birth but becomes evident in later life as behavioral disturbances. Since the mechanism involved does not appear to be immunologic and therefore not allergic, it is important to explore the field of pharmacology to determine the nature of the physiological disturbance. Since behavioral disturbances can be related to malnutrition, the field of nutritional science must be explored.

Finally, the clinical observation that biochemical aberrations can alter behavioral patterns should have important implications for the behavorial sciences—psychiatry, psychology, as well as the special sciences.

In closing, I should like to state that perhaps the suffering of the millions of troubled children will serve to a good and lasting purpose by forcing science to explore all facets of the problem which in turn should contribute to a better understanding of the behavior of man. With the recommendation of this august committee to provide funds for the support of both the clinical and research aspects of the program, I am confident we can successfully resolve this very critical problem.

Thank you.

Senator KENNEDY. Thank you very much.

Doctor, what do you think is really necessary for a final answer on this question?

Obviously, your initial studies and the work have been enormously impressive and rather hopeful.

What do you think is really necessary to develop some conclusive answers on it?

What do you advise us?

Dr. FEINGOLD. What I would advise is this.

We have two problems. We have the immediate urgent clinical problem, taking care of these children. We know it is empirical, if we take them off drugs, it will help at least 2 million children. And the second problem is research, research involves many disciplines. I think we have to start now.

There has been an interagency panel established to study the problem.

I think what is necessary for this panel to have, first, authority to act, it needs funds to act, and my understanding is, as I met with the panel, that they have no jurisdiction.

I met with Commissioner Schmidt on June 11 of this year. We discussed this matter. He was very receptive to the concept of establishing an interagency panel. As a matter of fact, there have been two meetings.

Commissioner Schmidt also at this time recommended that all funds necessary for implementing that program be channeled through this interagency panel rather than through each individual agency.

I would add to that, if I may, that there be a Director, or whoever is in charge of this panel, be an officer or someone under the Secretary of Health in the Office of the Secretary rather than a member of the panel itself. That is what my recommendation is.

I think, by coordinating all the disciplines, I do not think we are going to achieve the success and resolve this problem by having each individual agency operate separately, because they have overlapping of funds.

Senator KENNEDY. What should this panel do?

Should they be required to do the kind of research and study in the areas which you have outlined here?

Dr. FEINGOLD. I think the urgent part is seeing what can be done to encourage the establishment of a parents' group to have them take care at the grassroots the empirical application of the diet. Give it a try. Those children who respond, we have to look at very carefully and study the problem to find out what the chemicals are.

There are other epidemiologic agents. There must be. Call in all the disciplines. I think it is important, in addition, to call in industry and have the cooperation of industry and say we have a problem and we want to work with you and see what we can do to resolve this. We are not fighting industry. It is not our intention to fight industry. It is our intention, all of us, to cooperate, to work on this very serious crisis we have in this country and throughout the world, for that matter.

Senator KENNEDY. Ultimately, if these experiments support your early conclusions, you think it would be enormously valuable and helpful to have a logo device on the various foods to indicate there are special additions in the food?

Dr. FEINGOLD. I think it is important to have a logo as quickly as possible.

As a matter of fact, there is a group establishing a foundation, a group of parents who have had children responding successfully, the logo will be registered and licensed to the processors or food distributors which care to use it.

I think it is imperative that we get that started right away. One of the great problems we have is the parents do not know what foods are available to them.

Very quickly, any infraction upsets the child. It is particularly a hazard in the older children who have a tendency toward delinquency. Once they are off the diet, they immediately revert to lying, stealing, antisocial behavior.

Senator KENNEDY. Well, thank you very much.

Dr. FEINGOLD. Thank you.

[The prepared statement of Dr. Feingold and other material submitted by him follow:]

Statement before the Senate
Subcommittee on Health
Senator Edward M. Kennedy, Chairman
by

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Hyperkinesis and Learning Disabilities (H-LD)
Linked to the Ingestion of
Artificial Food Colors and Flavors

by

Ben F. Feingold, M.D.*

Mr. Chairman, members of the Committee, over the past several years I have discussed with various groups throughout our country as well as abroad one of the most critical problems of our contemporary culture, namely, hyperkinesis and learning disabilities (H-LD), but more specifically hyperkinesis and learning disabilities linked to the ingestion of artificial food colors and flavors.

This morning I consider it my good fortune and singular privilege to have the opportunity to discuss this important subject with so distinguished and influential a body as this committee which has the authority to initiate the procedures necessary for the early resolution of this crisis.

The magnitude of the problem can be appreciated with the knowledge that 10,000,000 children in this country are considered deficient in their learning abilities. Of these children approximately 5,000,000 or perhaps even 6 or 7 million are hyperkinetic; and of this number, conservatively 2 million children are victims of the promiscuous practice of treatment with behavior modifying drugs, e.g. the stimulants, amphetamine and Ritalin; tranquilizers like Stelazine and Mellaril; and the antidepressants, Elavil and Tofranil. And now new products are being added to this armamentarium of drugs to be used in conjunction with the stimulants to complete the job of making a zombie of the child.

The pervasiveness of the problem is also generally recognized. It is not limited to the elementary school grades, but involves individuals of all ages -- from early infancy through childhood, post puberty to adolescence, into adult life.

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I doubt that the problem is unique to our California schools, where at the Cañada Junior College just south of San Francisco, a group of 20 teachers is being briefed in preparation for 50% of the freshman class of 1975 who will require remedial learning.

You have no doubt learned from the press that the University of California at Berkeley, a very prestigious university, has 50% of the freshman class enrolled in a special class for English, called "Bonehead English".

In addition, there are literally thousands of students on the Berkeley campus with various learning deficits involving students at all grades, including the doctoral level. I understand a similar situation exists on most university campuses throughout the country.

This condition on the campuses is consistent with the decline in rating scores on the Scholastic Aptitude Tests since 1962. Over the past twelve years the scores on the verbal test have dropped from 487 to 440, while those for the mathematics tests have dropped from 502 to 487. Last year the tests given to 1,000,000 high school students indicated the scores are continuing to fall.

We must also be cognizant of the growing trend among law officers, social workers, psychologists, psychiatrists and educators to attribute to behavioral disturbances and learning disabilities in childhood the rising incidence of antisocial behavior, delinquency and criminality among adolescents and adults.

In the November 1974 report of the California Legislative Select Committee on Juvenile Violence there is cited the following:

(1) The number of juveniles arrested in California for crimes against persons (which includes homicide, robbery, assault and forcible rape) rose sharply between 1968 and 1973 (56.8%), compared with a decline (10%) in all other arrests.

(2) It is generally viewed that delinquent youth come from broken, cracked or fractured homes where the parents are incapable and unable to create a satisfactory

child-rearing atmosphere. This view is not substantiated by this committee.

(3) Any time a child comes into conflict with school or society, something has been ineffective with that child. The majority of troubled students have failed from the beginning of their school experience, are angry with themselves, the school and their parents.

(4) There is an important connection between the school experiences a child receives and his behavior. Improper schooling is a big contributor to juvenile violence.

My later comments shall indicate that this statement is not valid.

I feel confident that if an epidemic of similar proportions were attributed to an infectious process, e.g. encephalitis or polio, there would be greater public awareness and also a demand for not only adequate treatment but also a program for prevention.

Hyperkinesis is synonymous with hyperactivity. Hyperactivity is not a precise and distinct clinical entity but rather a constellation of signs and symptoms, which are listed in Table I. Although there are many characteristics of this behavioral disorder, since hyperactivity is usually the dominant feature, the disturbance is commonly labelled the "hyperkinetic syndrome" or the "hyperkinetic impulse syndrome". Actually, some children are not hyperactive, in which event the condition may be labelled by any one of several titles, as listed in Table II.

All the characteristics listed are not usually observed in any one child. More commonly, each child presents an individual mosaic of these features which will vary from child to child. In addition, the pattern may change from day to day and at times even from hour to hour. This great variability and lability of the clinical picture has defied attempts to organize the various manifestations into homogeneous patterns for the purpose of correlating with a specific etiology which would permit a more precise diagnosis and a rationale for management.

The term hyperkinesis is of comparatively recent origin, actually about 1957.

The clinical pattern has been reported in medical literature as early as 400 B.C. and perhaps earlier. Throughout the Middle Ages and as recently as the early 20th century behavioral disturbances labelled as "Tanzruh' (dance mania), St. Vitus' Dance, and chorea minor are suggestive of the hyperkinetic syndrome.

The epidemic of encephalitis following World War I left in its wake a high incidence of brain pathology. The clinical pattern associated with this brain damage was reported by Kahn and Cohen in 1934 with a description that is quite similar to what today is labelled the hyperkinetic syndrome. On the basis of these observations it became common practice, even in the absence of demonstrable brain pathology to attribute to organic brain damage any child with similar symptoms. The studies of Strauss and his associates through the 1950s abetted this concept.

Over the past several decades, in the long list of terms applied to the condition, there is considerable overlapping which has led to a great deal of confusion in the voluminous literature accumulated during this period.

As recently as February 1973 a prestigious panel on Minimal Brain Dysfunction sponsored by the New York Academy of Sciences resolved nothing. Hyperkinesis is still no better understood in spite of the tremendous volume of basic research and clinical observations. Perhaps the only advance over the past ten years has been the recognition that the hyperkinetic syndrome does not necessarily indicate organic brain damage. This has led to abandoning terms, e.g. Brain Damage and Neurological Damage, which have been supplemented with the milder term Minimal Brain Dysfunction, commonly identified as MBD which is an umbrella term encompassing practically all of the 38 categories listed in Table II.

This inability to classify the heterogeneous clinical patterns into homogeneous syndromes with specific etiologies has contributed in great measure to the lack of precise figures for the incidence of H-ID. Most reports are studies of learning disabilities attributed to behavioral deficits with a variety of labels.

Figures range from a low of 5% (Public Health Service publication No. 1646 entitled "Learning Disabilities Due to Minimal Brain Dysfunction: Hope Through Research") to a high of 28% reported by Eisenberg for a sixth grade population in a large metropolitan city, and in one report as high as 40%.

The State of California Department of Education makes special learning facilities available for 2% of the school population. No school district in California has a demand for such facilities of less than 5%.

The orientation of the observer -- whether a parent, a teacher, a psychologist, or a physician influences the interpretation of the behavior of these children and accordingly influences statistics for incidence. It is interesting that figures of psychiatrists on the average are lower, 4 to 10% of school children, while those of educators are higher, 15 to 20%.

Estimates indicating an increased incidence of hyperkinesis and learning disabilities are frequently challenged by attributing them to greater awareness of the problem rather than an actual increase. On the other hand, among parents, teachers, educators and other professionals dealing with children the consensus favors not only an actual increase but supports a progressive growth in the number of children involved with hyperkinesis and learning disabilities.

In establishing data for the incidence of H-LD in our schools, consideration must be given to the so-called "crowding syndrome" of experimental animal psychology. Observers in this field have repeatedly reported that rats confined to a limited space develop increased activity and aggression. This increased aggression is correlated with an increased concentration of serotonin in the brain that is considered an indicator of aggression.

Educators and teachers have observed a similar response among children in a crowded classroom. Under these circumstances it is reasonable to recognize that in a classroom with one or at the most two hyperkinetic and aggressive children who are constantly on the move and disruptive, not only do the normal children develop a higher level for their activity and expression of aggression, but even the teacher becomes hyperactive. After all, teachers are also human -- they are not made of steel.

It is important to consider this psychological observation in planning a school program for these children. In view of this phenomenon it may be advisable to reconsider the structure of the special classes for some of our educationally handicapped children. We may not be deriving the benefits we seek and may be defeating our objectives. It may be advisable to consider one-to-one teaching of these disruptive children which would be of mutual benefit to both the educationally handicapped child and his peers, not to mention the teachers.

To be considered in arriving at estimates for incidence are contributing factors such as socio-economic status, ethnic origin and environmental influences. Among the environmental influences which affect all aspects of the problem consideration must be given to the role of food additives and more specifically, artificial colors and flavors.

It is interesting to note how increased incidence and awareness of the problem is related to the growth of the color and flavor industry. The history of the growth of H-LD coincides with the rapid increase in the utilization of synthetic colors and flavors in our food supply. This has been particularly true since World War II and especially during the past decade. The forecast for the future is suggested by Senator Gaylord Nelson who places the present dollar value for this industry at $500 million, with a 1980 estimate at $750 million.

In conjunction with these estimates it is interesting to note that a graph projected for the estimated incidence of H-LD over the past ten years parallels the Standard and Poor's curves for the dollar value for soft drinks and synthetic flavors over the same period.

Our interest in food additives goes back about 20 years to the time our research laboratory was concerned with studies on the allergic reaction to flea bites. Very early in our experience we demonstrated that the allergic response to flea bites is induced by a low molecular weight chemical, i.e. a small chemical which in immunological terms is known as a hapten. Following this, our laboratory became concerned with studies on the behavior of low molecular weight compounds in the immune response. On the clinical side of our program we became involved in studying the adverse reactions to drugs and the adverse reactions to food chemicals.

Although on the surface these two problems may appear unrelated, they are actually the same. Except for terminology, there is no difference between a compound used as a drug and one used as a food additive -- they are both low molecular weight compounds with identical pharmacological potentials.

Following the thalidomide disaster, as of 1962 government regulations require for licensing of a compound used as a drug that the compound be tested on experimental pregnant animals. With few exceptions tests are carried out either at time of birth or within a few months thereafter for lethal effects of the compound, morphological anomalies, growth retardation and obvious organic dysfunction. They are never tested for behavioral effects upon the developing animal. It is important to recognize that not a single one of the thousands of chemicals introduced into our food supply as additives has been subjected to pharmacological studies. Yes, some additives have been investigated for carcinogenesis, teratogenesis, or mutagenesis, but never for pharmacological behavior.

Table III lists 2,764 compounds in 13 categories compiled from data gathered in 1965 by the National Science Foundation and National Research Council. In this discussion we are only concerned with two categories, the synthetic colors and the synthetic flavors.

This does not imply that the remaining categories do not induce adverse reactions. They do. Any compound, whether natural or synthetic can induce an adverse reaction if the individual has the proper genetic profile, i.e. predisposition. Accordingly, no compound is exempt. Therefore, each chemical introduced into our food supply must be evaluated on the basis of benefit compared with risk.

Since food colors and flavors constitute about 80% of all the additives used, they are the commonest cause of the observed adverse reactions affecting practically every system of the body. Colors and flavors are not essential to our food supply. They have merely a cosmetic or aesthetic function. They have no nutritive value. On balance the risks for colors and flavors far outweigh the benefits.

Our first observation of a behavioral disturbance attributed to the ingestion of artificial colors and flavors was in a woman who reported to the Allergy Department complaining of angio-edema, particularly about the eyes. The condition was attributed to the artificial flavors and colors, and accordingly, she was placed on an elimination diet. She responded quickly, but ten days later I received a call from the Chief of Psychiatry of our medical center, inquiring as to what we had done for this woman. He had her in psychotherapy for almost two years because of her behavioral disturbance -- her hostility toward her husband, her inability to adjust both at home and at work. She failed to respond to psychotherapy. However, on dietary management not only her angio-edema cleared, but her behavior improved. With any infraction of the diet both the angio-edema and the behavior disturbance returned.

The staff was alerted and other adults were observed, but our attention was directed primarily to the child with an identical response.

These children came to us for physical complaints, e.g. pruritus, urticaria, localized skin lesions, upper respiratory symptoms, etc. In the course of the management of these complaints, when they were attributed to the artificial colors and flavors, the parents reported that not only the physical complaint responded, but they also observed a marked improvement in behavior and scholastic achievement. Children who were poorly adjusted at home and at school because of aggression, impulsiveness, overactivity, and difficulty in learning very soon showed a rapid change in their behavioral pattern and their scholastic achievement.

Initially we were skeptical and surprised that dietary management could so dramatically influence the behavioral pattern. However, after analyzing the problem, our amazement and skepticism were dispelled with the realization that food additives like drugs are low molecular weight compounds. There are drugs that stimulate, drugs that depress, and drugs that modify the behavior of individuals. In clinical practice it is not unusual to modify behavior with drugs. Actually, this is constantly attempted in the treatment of hyperkinesis and MBD. We reasoned that among the thousands of chemicals added to our food supply there must be some compounds that influence behavior.

To investigate the condition more closely, we reached out to obtain children whose primary complaint was behavior and placed them on the diet.

We were amazed at the dramatic responses of some of these children to dietary management. Children with a history of hyperactivity dating to early infancy, in some cases on medication, e.g. amphetamines, Ritalin or tranquilizers for several years, showed a complete transformation in their behavior pattern within days or weeks, which was followed by a rapid improvement in scholastic achievement. Equally dramatic is the ability to "turn on" the behavioral pattern within 2 to 4 hours following any deliberate or fortuitous infraction of the diet and the ability to "turn off" the pattern following complete compliance on dietary management.

Before discussing the response to dietary management, it is well to consider briefly the nature and characteristics of H-LD.

In early infancy restlessness, head banging, rocking, fretfulness, crying and sleeplessness are dominant features. Not infrequently, these children are misdiagnosed as colicky, and are subjectec to frequent changes in formulae.

At nursery school and kindergarten impulsiveness and aggression become apparent, while it is usually during the first and second school grades that the fully developed pattern becomes evident. A short attention span coupled with impulsiveness and aggression propels the child every few seconds from one activity to another, frequently with the accompaniment of incessant jabbering. This behavior disrupts the classroom and disturbs both peers and the teacher.

The constellation of characteristics persists through puberty, into adolescence, and at times even into adulthood. However, not infrequently as the child passes through puberty the hyperactivity may diminish or complete fade out. The remaining characteristics with all the accompanying psychological deficits, e.g. antisocial behavior, lying and stealing, persist. It is this evolution of the pattern that supports the growing tendency among educators, psychologists, psychiatrists and law officers to attribute to hyperkinesis in childhood the rising incidence of antisocial behavior, delinquency and criminality among adolescents and young adults.

Although the children are bright, they frequently fail at school which surprises the parents and frustrates the child. Parental surprise may derive from the difference in behavior at home as compared with school where the child must contend with a structured classroom environment, the need to learn and the competition with peers.

Frustration of the child ensues from the inability to perform to the full level of his competence. As a result, as these children approach adolescence, they are frequently withdrawn and suffer from a very low self-esteem.

It is important to recognize that this entire behavioral pattern is beyond the voluntary control of the child. He does not choose to be a failure, nor does he want to be bad. It is as though something within is driving him. He is like a revved-up motor with the throttle stuck.

Discipline achieves nothing but invites rebellion and further frustration which precipitates displays of temper and tantrums.

Over the past several years we have observed several hundred children with H-LD. In addition, we have received reports from parents, teachers, psychiatrists, psychologists, and pediatricians reporting on the favorable responses to dietary management. Favorable responses to dietary management have been reported for hundreds of children from practically all 50 states as well as Canada, England, France and Germany. A psychiatrist with the Ministry of Health of New South Wales, Australia has reported favorable results with dietary management.

A double blind crossover study was funded by the National Institute of Education to evaluate my hypothesis. This program was under the direction of Dr. C. Keith Conners of the University of Pittsburgh with myself as consultant. The study reported to him as follows:

> The results of this study strongly suggest that a diet free of most natural salicylates, artificial flavors and artificial colors reduces the perceived hyperactivity of some children suffering from hyperkinetic impulse disorder. Teachers who observed the children over a 12-week period without knowledge of when the child started his diet and without knowledge of the fact that there were two diets which were employed, rated the children as less hyperactive while the children were on the diet recommended by Feingold. The difference obtained between the ratings when the children were on the K-P diet and when they were on the control diet would have occurred by chance only 5 times in one thousand. Similarly, the teachers rated the children as significantly improved over the baseline period at the beginning of the study while on the K-P diet but not while on the control diet.
>
> The results from ratings by parents are slightly different in that parents do not detect a difference in behavior between the K-P and control diets, although they note the effect as compared with the baseline period. The fact that the parents do not detect a difference between the two special diets could mean that subjective factors associated with a change in diet of any kind mask whatever therapeutic effect might be present in the K-P diet. This interpretation is supported by the fact that whereas the baseline means for parents and teachers are very similar (16.3 and 16.5, respectively), the control diet means are somewhat different (15.7 vs. 17.2).
>
> Another possibility is that the children are in fact not noticeably different at home, but are observed to respond better in a more structured situation where task expectations are clearly established, and where the teacher has a long baseline of

comparison of the same children over many months. Similar findings of weak or marginal effects on behavior as rated by parents in contrast to clear effects noted by teachers has been found in drug studies with hyperkinetic children. It has been generally assumed that the demands on the child's attention and goal-oriented behavior are greater in the classroom, and therefore that any improvements in these areas will be more evident.

It was found in this study that the bulk of the positive changes noted by both parents and teachers occurred in the group that started with the control diet and then switched to the experimental diet. Such an effect could be due either to the fact that the more responsive children happened, by chance, to fall into the sequence involving the control diet first: or the results could be due to the fact that the observers have a clearer basis on which to judge improvement after the control diet has failed to produce any noticeable changes. Although this finding weakens the argument that the obtained differences are reflecting the K-P diet rather than some nonspecific factors, it should be noted that such findings are quite common in psychopharmacologic research involving crossover designs. For example, in a double blind crossover study involving dextroamphetamine and hyperkinetics (Conners, Eisenberg, and Barcai, 1967), the following results were obtained on the teacher questionnaire (using a somewhat different set of items):

	Pre-Treatment	Dexedrine	Placebo
Drug 1st (N=28)	29.1	20.6	26.00
Placebo 1st (N=24)	22.6	12.8	21.2
Combined	25.6	16.7	23.6

It is clear that the drug effect is much more pronounced in the group which received placebo first. Thus, even when objective measures substantiate improvement in behavioral functioning in the first period of evaluation, the teachers may be less aware of the improvement until they see the lack of improvement on another treatment.

Inspection of the individual ratings of children in the study shows that only four or five of the children were seen as improved by both parents and teachers. This fact is apparent from inspection of the clinical global impressions which took into account both parent and teacher effects. The findings suggest that there may be a small subgroup of hyperkinetic children who are showing the changes induced by the K-P diet. Further research will be required to determine if such children are physiologically different from non-improvers. Another possibility needing further evaluation is that somehow the blind of the experiment, the bias of the parents, or communication between parent and teacher regarding the diets served to bias the results in the children rated as improving. It seems unlikely on the face of it that teachers would detect a significant effect when they are unaware that two diets are involved. On the other hand, if enthusiastic parents communicated to teachers when the diets were changed, the obtained results would be entirely spurious.

It is important to note that dietary compliance and degree of difficulty following the diets were comparable for the control and K-P diets. The K-P diet may have been slightly more difficult to follow, but there were also slightly fewer infractions, suggesting that the effects are unlikely to reflect any real difference in the difficulty of maintaining the child on the diets.

The experiences to date indicate that between 30 and 70% of the children respond to dietary management, or an average of 50%.

Our present observations indicate there are two groups of individuals affected by the artificial colors and flavors -- a primary group and a secondary group.

In the primary group the responses are dramatic, rapid and complete.

In the young infant the commonly observed characteristics, e.g. head hanging, head knocking, rocking, crying, irritability and sleeplessness show rapid clearing, often within 24 to 36 hours. In these children there has invariably been a history of pediatric vitamin drops which are artificially colored and flavored.

In the older child with primary involvement the improvement is also very rapid and dramatic. Initially, there is a loss of hyperactivity, aggression, impulsiveness, which is accompanied by an increased attention span. The child no longer flits from object to object or from project to project. Instead of fretfulness, whining and temper tantrums the children are affectionate, affable and very responsive to directions. This is accompanied or soon followed by improvement in muscular coordination. With improvement of gross muscular coordination there is a loss of clumsiness. They can ride a bicycle, swim and participate satisfactorily in sports. Fine muscle coordination is reflected in improved writing and drawing, the ability to button clothes and tie shoes, improved facility in reading and in speech. Disturbances in cognition and perception are usually the last to respond. With increased attention span which permits greater concentration, a rapid improvement is observed in scholastic achievement.

In the secondary group, the disturbances induced by the additives seem to be superimposed upon underlying pathology, either gross brain damage or a physiological disturbance. For example: a child with phenylketonuria (PKU) associated with hyperkinesis of such an extreme degree that although institutionalized, management was very difficult -- actually almost impossible. Following the elimination diet, the hyperactivity cleared, permitting the child to be managed with little or no difficulty. Naturally there was no effect upon the PKU.

Another example is that of an 8 year old child with a history of seizures dating back to 1 year of age, occurring every night about one hour after getting to sleep. Following dietary management, the seizures cleared completely, but cognitive and perceptive disturbances persisted. This child has not been observed over a sufficient period to determine whether the latter deficits will ultimately improve with continued elimination of the colors and flavors.

A third very important example of what may be secondary involvement is that of identical twin boys about 9 years of age with a diagnosis of petit mal. The children failed to respond to anticonvulsant drugs such as Dilantin but did respond favorably to amphetamine. Performance at school was poor. Following management with the elimination diet, the seizures cleared, the medication was discontinued, and the children performed well at school.

Age seems to be an important factor influencing the response. The younger the child, the more rapid and more complete the response. The infant whose behavior may be induced by vitamin drops with artificial colors and flavors will show a response within 24 to 36 hours. Between 3 to 5 years of age a response may occur after the third day on dietary management, while the average prepubescent child will require 10 days to two weeks. Occasionally, a longer period of dietary management is required as with children who have been medicated with long-acting amphetamine spansules and may require up to 40 days before a response is observed.

After puberty, the residual deficits, particularly in cognition and perception are observed, while in adolescence the number of successes seem limited. Occasionally, an adolescent of 16 to 18 years of age will show an improvement in the behavioral pattern with a residual of learning ability, but the majority at this age level fail to respond.

The ability to "turn on" and "turn off" the behavioral pattern has already been indicated.

The other dominant features are the predisposition for boys over girls, usually 5 or even 9 to 1; the involvement of only one child in the family; and the usual occurrence of the disturbance in children with a normal or high IQ.

Three patterns of response have been observed. First, the children who show a rapid and complete reversal of the behavioral pattern with no residuals, and second, the group who show an improvement in the behavioral pattern, i.e. loss of aggressiveness, impulsiveness, hyperactivity, improved motor coordination and lengthened attention span, however, with deficits in cognition and perception which interfere with learning ability. The third group includes the complete failures.

In the absence of basic studies on the food additives we can perhaps find guidelines for some interpretations of the clinical pattern by drawing upon observations reported by other branches of science, such as pharmacogenetics, a comparatively new discipline of about ten years, and the newly emerging science of behavioral toxicology with its subdivision behavioral teratology.

Studies in the field of genetics over the past few decades have demonstrated that each person has a unique "biological individuality" that determines a "pharmacological individuality". The pharmacological reactions of drugs depend to a great degree upon proteins that have a high degree of specificity. The quantity and the quality of these proteins can be altered through genetic mutations which influence the metabolism, their binding abilities and the receptor interactions.

There are a number of metabolic variations which are actually not abnormalities, since under normal conditions the individuals manifest no disturbances. However, in the presence of certain drugs they express their potentially dangerous character.

For example: the abnormal hemoglobin Zurich, which is characterized by the replacement of a histidine residue by arginine at the 63-position of the amino acid sequence of the beta chain of hemoglobin. The molecule is abnormally sensitive to oxidative denaturation but not to the point where this occurs spontaneously at an appreciable rate. Under normal conditions heterozygotes show no unusual symptoms, aside from a slightly shortened life span of the erythrocytes. However, when such patients are given sulfonamides or other oxidant drugs, methemoglobinemia develops. The hemoglobin denatures and precipitates which results in a fulminant hemolytic anemia. Similar adverse effects have been observed with some other abnormal hemoglobins.

Another example is inherited deficiencies of the enzyme glucose-6-phosphate dehydrogenase (G-6 PH), a condition thought to affect some tens of millions of people. Here again the pathology is essentially drug dependent, and hemolysis results from a number of compounds, e.g. the anti-malarial primaquine, para-amino-salicylic acid, phenacetin, the sulfonamides and also certain constituents of the broad favus bean. It is interesting to note that the gene carrying the determining characteristics for this enzymatic disorder is on the X-chromosome. This explains the greater frequency of the enzyme deficiency and drug sensitivity among males. This observation is highly suggestive that in H-LD the X-chromosome may be involved, which could explain the overwhelming preponderance among boys, as well as the occurrence in only one boy in a family.

A still further example of the contribution of genetics to the variability of drug metabolism is that observed with Isoniazid (INH) which is currently in common use for the treatment of tuberculosis. Very early in the use of INH clinicians observed wide variations in the metabolism of the drug, whether measured by the decrease in serum level of INH or by the rate of urinary excretion in the form of acetyl INH. The problem was resolved following the demonstration that the general population is divided into two genetic groups, namely, "slow inactivators" and "rapid inactivators". INH inactivation is controlled by two autosomal alleles at a single genetic locus identified as R (rapid) and r (slow). Both homozygotes and heterozygotes for the rapid allele (RR and Rr) are rapid inactivators, while only the slow homozygotes (rr) are slow inactivators. In other words, slow inactivation of INH is a recessive trait.

It is also interesting to note that slow inactivators (rr) are also more likely to show toxic effects from two drugs chemically related to INH — the antidepressant phenelzine, a mono-amine oxidase inhibitor, and the antihypertensive hydralazine.

This observation raises another important point relative to H-LD and the artificial colors and flavors, namely, the possibility of cross reactivity among each group of chemicals, resulting in more than one color or more than one flavor to be at fault in the same individual. This is supported by the recognition that the colors are derived from four basic structurally related groups, while the flavors, although occurring in the thousands, also show a close structural relationship. Accordingly, the broad exclusion provided by the elimination diet is necessary for successful management.

The Lesch-Nyhan syndrome, which has been described less than ten years ago, may also serve as a guide in studying the possible genetic basis for H-LD as related to artificial colors and flavors. In this disease the defect which involves a deficiency of the enzyme hypoxanthine guanine phosphoribosyltransferase (HPRT) is an X-linked recessive condition that occurs exclusively in males. The importance of the Lesch-Nyhan syndrome as a guide in studying H-LD is twofold:

(1) The involvement of the X-chromosome with the exclusive implication of males.

(2) This is the first disease in which an identified biochemical abnormality can be associated with a specific aberrant pattern of behavior, namely compulsion and aggression.

Although environmental influences have not been demonstrated for Lesch-Nyhan disease, nevertheless, it is conceivable that other variations of the X-chromosome or perhaps polygenic alterations may be responsible for environmentally induced behavior patterns, e.g. the artificial colors and flavors in H-LD.

In addition to metabolic disturbances and enzymatic variations, anomalies of the receptor sites can be at fault. Receptors may exhibit either increased or decreased sensitivity as is observed in coumarin tolerance and vitamin K activity.

It is also possible that the involvement of children with either normal or high IQs may be on a genetic basis.

Educators and child psychologists generally recognize that in the early years and through the preschool years girls exceed boys in learning achievement. By the beginning of school, however, there are no longer consistent differences. It is also at school age that the pattern of H-LD becomes apparent in most children. This could also be an expression of the pharmacological activity of the artificial flavors and colors exerting a repressive action upon normal physiological action.

On the basis of the observations in pharmacogenetics, it is conceivable that H-LD is an expression of the pharmacological activity of artificial colors and flavors in individuals with genetic variations. It is possible that the adverse response to these chemicals exerts a repressor effect which prevents the normal expression of these children. A repressor effect could explain not only the rapid, dramatic improvement in the clinical pattern which follows elimination of the chemicals, but also the speedy recurrence of symptoms, within hours, following ingestion of the additives.

The partial response to dietary management observed in some children; the high incidence of complete failures to respond in adolescents; and the role of age as a determining factor in the behavioral response are not explained by pharmacogenetics. However, answers to these problems are suggested by behavioral toxicology and its subdivision behavioral teratology.

We learn from these two disciplines that any compound may cross the placental

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barrier either by simple diffusion or by transport. Since the mechanism for detoxifying and excreting noxious substances which cross the placental barrier has not developed in the fetus and the newborn, the developing organs are very susceptible to damage from such chemicals and from radiation. In addition, it is pointed out in behavioral teratology that teratogens have a special affinity for developing brain centers. The alterations in the brain centers induced by teratogens are manifest as behavioral alterations.

It must be recognized that behavior is as susceptible to teratogenic effects as other developing systems. However, unlike the gross somatic abnormalities of conventional teratology, the subtle behavioral abnormalities are not readily evident unless revealed by special tests during post natal life. Or at times a gross neurological or biochemical lesion may remain dormant and not become manifest until late in life as a behavior disorder or functional disturbance. It is for this reason that the behavioral alterations induced by teratogens are frequently not apparent in early life, but only after the individual is older. An additional complicating factor is the observation of behavioral disturbances with low doses of teratogens in the absence of gross functional or structural birth defects.

Subtle delayed effects are difficult to detect and may require evaluation over a lifetime in a controlled environment.

In view of the observations in the fields of behavioral toxicology and teratology, it is conceivable that the behavioral disturbances observed at any age may be an expression of neurological damage induced during gestation. The dramatic responses in the younger child may be associated with incomplete nerve damage, and of a magnitude which permits the compensatory mechanism of the developing brain to adjust completely following removal of the offending irritating chemical, e.g. the colors and flavors. On the other hand, the persistent residual deficits, particularly in the older child, may be an expression of permanent neurological damage. If this is true, it could explain the high incidence of failures following dietary management of the post pubescent child, and particulary the adolescent.

It is also conceivable that the cognitive and perceptive centers of the brain are more susceptible to teratogenic effects, since they complete their development later than the motor centers. This could explain the favorable response of the behavioral pattern to dietary management with residuals of cognitive and perceptual deficits which interfere with learning.

It is evident that in all situations age is a very determining factor. As our clinical observations point out, the younger the child, the more rapid and more complete the response, which is consistent with the chronological development of the brain.

In addition to the primary change induced by the teratogenic effects of the chemicals, consideration must be given to the secondary conditioning of the individual resulting from the constant reinforcement induced by the conscious effort to cope with the environment. This is observed particularly in the post pubescent and adolescent individual who is constantly frustrated by his failure to control his behavior which does not permit him to adjust to his environment and perform at his full potential. This leads to withdrawal, a lowered self-esteem, antisocial behavior, e.g. lying, stealing, abusiveness and aggression which ultimately can be manifest as delinquency and criminality.

Allergy must also be considered in the dietary management of the children. Since allergy is an inherited constitutional state affecting 25% of the human race, it is reasonable to expect 25% of all children with hyperkinesis and learning disabilities to be allergic. However, since the mechanism involved with the colors and flavors does not seem to be immunologic, i.e. it is not allergic, the majority of children with concomitant allergy will respond to dietary management without any special attention to the control of the allergic symptoms, if present. In a small percentage of allergic individuals the diet is not operant unless the allergy is controlled. In a still smaller percentage of hyperkinetic allergic children the allergy seems to be the primary factor, with no involvement of the food chemicals. In such cases management must be directed to control of the allergy symptoms.

It is interesting to note that the pattern usually associated with allergy is the opposite of hyperkinesis. The allergic child is usually pale, listless, fatigued, wan, with a pinched expression -- the pattern of the so-called Tension-Fatigue syndrome -- so much so that when a child presents with this pattern, we usually suspect an allergic etiology, while with hyperactivity, aggression, impulsiveness and short attention span, hyperkinesis, a non-immunologic mechanism is considered.

Children who have been on drugs for years can usually discontinue the medication. It is usually advisable to discontinue all medications within 24 to 48 hours after starting the elimination diet. When the diet is effective, the stimulating drugs, e.g. amphetamines and Ritalin may lose their paradoxical effect which may lead to an aggravation of the behavioral pattern. In addition, for some children the small amount of dye coating the tablet may be sufficient to induce hyperactivity. Children under treatment with dextroamphetamine spansules, a long-acting drug, may require up to 40 days before a favorable response is observed with dietary management.

Drugs such as the stimulants amphetamine and Ritalin; the tranquilizers Stelazine and Mellaril; and the antidepressants Elavil and Tofranil are very frequently prescribed for management of the H-LD child. At best, drug therapy is only a palliative measure. They do not cure the child; they do not correct the cause for the behavioral disturbance.

MANAGEMENT WITH THE ELIMINATION DIET

A brief review of the historical development of the elimination diet will explain its structure and application.

Our clinical interests were initially concerned with adverse reactions to drugs and adverse reactions to food additives, more specifically, artificial colors and flavors. Both are low molecular weight compounds, and in this respect they are identical.

Because of the widespread use of aspirin, reactions to this drug are quite common. In managing the aspirin sensitive patient, we observed, as have many other investigators about the world, that discontinuing aspirin did not always lead to a clinical response. About 15 years ago we learned that a number of foods contain a natural salicylate radical. On the basis of this observation we constructed a diet eliminating all foods containing a natural salicylate radical and also seven artificial flavors that contain a salicylate radical, for example, mint. The application of this diet led to increased success in the management of the aspirin sensitive patient, but not entirely.

The next step was the observation by us and by a number of clinicians about the country that aspirin sensitive patients were also intolerant to tartrazine (FD&C yellow #5), a very ubiquitous dye in our foods, beverages and medications. Aspirin sensitive patients react to tartrazine, while tartrazine sensitive patients react to aspirin, although aspirin and tartrazine have no chemical structural similarity.

On the basis of this observation the diet was expanded to provide for the elimination of all items containing tartrazine (FD&C yellow #5) as well as all foods with a natural salicylate radical and flavors with salicylates. Again we observed an improvement in the dietary management of the aspirin sensitive patient, but not entirely.

The next observation of importance was that of Vane and Ferreira who reported that aspirin and indomethacin inhibit prostaglandins (PGE_2), a widespread mediator in body tissues. In addition, aspirin sensitive patients react to indomethacin and vice versa. Again, it must be noted that aspirin and indomethacin have no chemical structural relationship. In other words, they do not look alike.

The cross reactions observed clinically with aspirin, tartrazine and indomethacin, which are unrelated in chemical structure, led to the hypothesis that among the several thousand colors and flavors in our food and drug supply there must be other chemical compounds which although not related structurally, may induce identical adverse clinical responses. Accordingly, a diet was constructed eliminating (1) all foods with a natural salicylate radical, and (2) all synthetic colors and flavors. This is the diet applied in managing the children with H-LD as well as all patients with an adverse response attributed to artificial colors and flavors.

The mechanism by which the chemicals cause the adverse reaction is not known. Several hypotheses have been proposed, but none have been confirmed. However, there is general agreement that the adverse reaction to the food chemicals is not immunologic, which means it is not allergic in nature.

In the absence of an explained mechanism there are no tests to determine an individual's intolerance to the food chemicals. In addition, in view of the several thousand chemicals involved and the possibility that many of the colors and flavors cross react, a compound by compound identification is not practical at this time. In view of these circumstances, dietary management of the adverse reactions to the synthetic colors and flavors is purely empirical. Empiricism is not a rare experience in clinical medicine -- actually, it is rather common and particularly when it is concerned with the pharmacological behavior of drugs. The precise mechanism involved in the action of most drugs is not known. For example, very little is actually understood regarding the behavior in the body of aspirin, a widely used medication. There are some observations on aspirin that suggest hypotheses, but there is no absolute or precise understanding of how the drug operates.

Although the diet is very simple, the initial reaction of the parent is often one of bewilderment and apprehension. Bewilderment because of the high incidence of artificial colors and flavors in our processed food supply and apprehension because of a fear that very little may be available to eat. Actually, the diet is extremely liberal and nutritious. Except for the fruits and two vegetables with natural salicylates, no food is prohibited provided it contains no artificial colors or flavors. This may require a little careful reading of labels at first, but very soon the parent and at times even an older child learns that many permissible foods are available on the market. It may be necessary to prepare some foods at home to insure their freedom from artificial flavors and colors. These include items such as pies, cookies, cakes, pastries, candies and ice cream. However, in some areas these are obtainable in the markets.

A short period of investigation of the food supply in the community will reveal the sources of all types of permissible foods. It is usually not necessary to rely upon the health food shops. The information gathered, added to a few menus and recipes, can be extremely helpful to a young parent in tiding over the early weeks of management. A program of strict adherence to the diet should be rewarding in about 50% of the H-LD children. Once a favorable response is observed, both the parents and the child become aware that not only the cause for the behavior is known, but also a cure is available. Many parents harbor a sense of guilt over the child's behavioral problem and failure to perform at school. The informed medical or paramedical practitioner can play an extremely important role through counselling and guidance in allaying such fears which will correct unjustified emotional disturbances.

As for the children, in most cases they are pleased to adhere to the diet which avoids the need for medication, permits them to adjust both at home and at school where they enjoy the ability to perform to their full potential. Since they are bright children, they are very soon listed in the upper percentile of the class.

The dietary management of the hyperkinetic child resolves itself into two programs. First, the clinical application of the diet and second, improving our understanding of the problem through research.

The need for clinical application of the program is both critical and urgent. There are millions of hyperkinetic children who are disrupting their homes and their classrooms. They are failing scholastically and are in constant conflict with their peers. As a sequel, antisocial behavior develops, characterized by lying, stealing and various degrees of violence which in many cases can lead to juvenile delinquency. Although the diet must be applied empirically at present, it still offers promise of a favorable response in approximately 50% of the troubled children. This means that we should anticipate correcting the problem for several million children in this country.

Fortunately, the diet is very liberal and nutritious. Instead of adding a compound or a drug, we eliminate the harmful chemicals and discontinue all medications. The risk is nil, and the potential benefits are great.

It is our judgment that successful dietary management cannot be mandated. It must be generated from the grass roots. Toward this objective we are promoting the establishment of associations of parents at the school or school district level. These voluntary organizations will permit parent interaction offering a vehicle for the exchange of experiences, menus, recipes as well as provide information on permissible foods available in the local markets. Such an association is already functioning in Bridgeton, New Jersey.

With the recognition that a single infraction can induce a return of symptoms within 2 to 4 hours, absolute compliance with the diet becomes obligatory. Strict compliance frequently becomes a problem due to inadequate disclosure of chemicals on the food package and also the frustration caused by the hours required for checking labels which are frequently illegible and not understandable. The absence of pediatric medications free of artificial colors and flavors also complicates compliance.

To assist the consumer to expedite shopping we are advocating the adoption of a symbol or logo to appear on every package of food or beverage which does not contain artificial colors and flavors. The logo will place no restrictions upon the food processor beyond the regulations imposed by the FDA. The logo will offer the consumer a free choice between foods with and without the chemicals in question. In addition, the logo will permit the natural laws of the marketplace to operate -- the basic philosophy of a free society.

Research must involve many disciplines. Studies in the field of genetics may explain the selection of the individuals who react adversely to chemicals and also the preponderance of boys over girls. Research can utilize the observations in the field of behavioral toxicology, a newly emerging discipline which has demonstrated that chemicals can induce intrauterine damage which is not apparent at birth but becomes evident in later life as behavioral disturbances. Since the mechanism involved does not appear to be immunologic and therefore not allergic, it is important to explore the field of pharmacology to determine the nature of the physiological disturbance. Since behavioral disturbances can be related to malnutrition, the field of nutritional science must be explored. Finally, the clinical observation that biochemical aberrations can alter behavioral patterns should have important implications for the behavioral sciences -- psychiatry, psychology, as well as the social sciences.

In closing, I should like to state that perhaps the suffering of the millions of troubled children will serve to a good and lasting purpose by forcing science to explore all facets of the problem which in turn should contribute to a better understanding of the behavior of man. With the recommendation of this august committee to provide funds for the support of both the clinical and research aspects of the program, I am confident we can successfully resolve this very critical problem.

BFF/mw
9/5/75

Table I

Descriptive Characteristics of Clinical Pattern of H-LD

1. Marked hyperactivity and fidgetiness
2. Compulsive aggression
3. Excitable -- Impulsive
4. Tolerance for failure and frustration is low
5. Short attention span -- Unable to concentrate
6. Exceptionally clumsy
7. Poor sleep habits
8. Cognitive disturbances
9. Perceptive disturbances
10. Normal or high IQ but fails at school
11. Boys are involved 7:1
12. Rarely more than one child in a family

Table II

Organic Terminology

Association Deficit Pathology
Cerebral Dysfunction
Cerebral Dys-synchronization Syndrome
Choreiform Syndrome
Diffuse Brain Damage
Minimal Brain Damage
Minimal Brain Injury
Minimal Cerebral Damage
Minimal Cerebral Injury
Minimal Cerebral Palsy
Minimal Chronic Brain Syndromes
Minor Brain Damage
Neurophrenia
Organic Behavior Disorder
Organic Brain Damage
Organic Brain Disease
Organic Brain Dysfunction
Organic Drivenness

Symptomatic Terminology

Aggressive Behavior Disorder
Aphasoid Syndrome
Attention Disorders
Character Impulse Disorder
Clumsy Child Syndrome
Conceptually Handicapped
Dyslexia
Educationally Handicapped
(California State Legislature AB464)
Hyperexcitability Syndrome
Hyperkinetic Behavior Syndrome
Hyperkinetic Impulse Disorder
Hyperkinetic Syndrome
Hypokinetic Syndrome
Interjacent Child
Learning Disabilities
Perceptual Cripple
Perceptually Handicapped
Primary Reading Retardation
Psychoneurological Learning Disorders
Specific Learning Disorders

Table III

Classification of Intentional Additives

1.	Preservatives	33
2.	Antioxidants	28
3.	Sequestrants	45
4.	Surface Active Agents	111
5.	Stabilizers, Thickeners	39
6.	Bleaching and Maturing Agents	24
7.	Buffers, Acids, Alkalies	60
8.	Food Colors	34
9.	Non-Nutritive and Special Dietary Sweeteners	4
10.	Nutritive Supplements	117
11.	Flavorings -- Synthetic	1610
12.	Flavorings -- Natural	502
13.	Miscellaneous: yeast foods, texturizers, firming agents, binders, anticaking agents, enzymes	157
TOTAL NUMBER OF ADDITIVES		2764

Va. Beach, Va. 23462
Feb. 19, 1974

Dr. Ben Feingold
Kaiser- Permanente Medical Center
San Francisco, Calif.

Dear Dr. Feingold;

I read the article about your diet for hyperkinetic children to my 10 year old son, [redacted], who put himself on your special diet Jan. 25. I am amazed at the results. Last weekend [redacted] sat quietly and built an airplane box kite, something he would never have had the patience to do before; he hasn't had a temper tantrum in over a week, while, before the diet, he had them every day--especially before school. His spelling, his worst subject, has improved noticeably. He has stuck to the diet in the paper religiously, except that he has had apple juice unsweetened, not realizing that apples would probably restrict apple juice too.

[redacted]s father and I are divorced, but his father sees him most weekends. After these weekends [redacted] would have terrible tantrums, when he was smaller he would pick fights with me and on one occasion even threw himself down the stairs. Last weekend he came home happy and normal for the first time. He had been on medication til he was about 5 years old when I quit giving it to him because it made him fall asleep, and then his father was away for almost two years--and in that time there was a noticeable improvement. [redacted] said last weekend that his Dad tried to talk him into eating some candy but he wouldn't take it, and on Valentine's Day he brought his school candy home to me.

He has had a learning disability since second grade, and was thoroughly tested by the Tidewater Rehabilitation Center and recommended for treatment at the Va. Beach Center of Effective Learning, where he has been on their waiting list for almost three years. They had found his trouble to be Audio perceptual. Yet his problem seemed to be more his attention span than listening. He can never remember how to spell words yet his I.Q. is 128. *He has luckily been in an ungraded elementary school, where his problem has usually been understood. But I have been going to school full time working towards a degree and haven't spent the time helping him that I should.

I intend to talk with his pediatrition about the diet. I have also noticed that foods need to be better labeled.

Please don't let anyone discourage you in your work, Dr. Feingold, I know you're on the right track. This may have a lot to do with "Why Johnny can't read." You know children must suffer from this if a little boy will put himself on a diet like this. But he said the other day, "You know, foods like this are pretty good." And they really are too.

Thank you for your interest in children with [redacted]'s problem. My best wishes to you.

Sincerely,

*I forgot to say that he was also tested by a psychologist and found to have no psychological problems--in fact, the psychologist said that for a child with [redacted]s background, he was exceptionally well adjusted as far as he could see.

Park Ridge, Illinois
July 31, 1973

Ben Feingold, M.D.
Kaiser-Permanente Medical Institute
San Francisco, California

Dear Dr. Feingold,

The report on your findings of the effect of artificial coloring and flavoring appeared in the *Chicago Tribune* on June 27, 1973. Because I have a hyperactive child who has been on Ritalin for almost four years, I was very interested in your findings. That same evening I discussed the article with my son and asked if he would be willing to try your method of behavioral control. I received an enthusiastic "Yes" (he is quite aware of his problem and dislikes the dependency of medication) and we began the next day.

The results have been astounding! From the third day of the diet, his behavior has been normal except for the times when he ate foods, unknowingly, containing artificial flavors.

I am anxious to know if your studies included school performance. Can I expect him to concentrate in the classroom as well as he did when on the Ritalin?

Could you please tell me, too, if when a product, such as canned soup, lists in their ingredients "flavorings", does that mean artificial or natural flavorings? Do you have a list of foods to avoid?

Thank you for your help in clearing up these matters.

Sincerely yours,

NOKOMIS, FLA., *August 25, 1975.*

DEAR DR. FEINGOLD: My husband and I are so very grateful for your extremely important research and thus for your book written on the subject of hyperactive children.

Our 7 year old son has been to two doctors and a psychologist, a neurologist and has been tested for L.D., and MBD and other areas also. He is a bright boy and sometimes a sweet lovable youngster. However his presistent behavioral problems, his anger, his frustration, his emotional conflicts are and have been as though someone controlled him by means of a (on and off) switch.

His story is a long involved and most frustrating one. When he got into school even more troubles were added. Our son indeed is a child very much affected by additives in today's foods.

Now that we are aware we are careful about his diet and have incorporated it into our family. I bake most all of what we eat from scratch. When he gets something that he should not have—the tension, anger, frustration and comprehension are at a very difficult level to cope with.

Our son has apparently different reactions to different colors—flavors etc.. Eg. He frequently drew ghosts, dreamed about them and in fact at times ghosts would be utmost in his whole realm for days at a time—no reasonable explanation why. We began his special diet in Feb. 74, and (ghost free) 2 months later was accidentally given Red Hawaiian Punch—result 2½ days of ghost drawings, dreams & etc. then no more until shortly after school was out he had some candy he hadn't had in over a year—once again 1½ days of recurrent ghost activities.

Also our son before the special diet had several bouts with ulcers in his mouth; 2 times so very bad I had him to the Doctor. He often had very foul breath from the time he was very young—no reasonable explanation. During this same period before Feb. 74 our son had very frequent episodes where his eyes bothered him in the sunlight—again diagnosed as no reasonable explanation only possibly a "Sun Phobia." Since his diet he's had no mouth ulcers, seldom foul breath and seldom eye problems. Again these problems have turned up when he's had something that is "off his diet."

There is so much to learn, so much more to this that I want to find out what I can. Is there any other way to learn more about your research findings? I feel there is much to learn and more to understand concerning this area of research. Many, many more parents and youngsters are going thru the same "Hell" we have been thru just trying to love and understand our boy.

God bless you in your great work—Please push on—Please let us parents know somehow what has been learned.

Thank you again and again,

——— ———.

ST. CLOUD, MINN., *May 24, 1975.*

Re name and address of physician familiar with K-P diet.

KAISER-PERMANENTE HEALTH CARE PROGRAM,
Kaiser Research Institute,
San Francisco, Calif.

GENTLEMEN: I have a five year old son who suffers from abnormal periods of frustration, negativism and worry, all of which result in crying and difficult behavior. Also accompanied with this behavior are almost nightly violent, traumatic nightmares leaving the boy emotionally and physically drained the subsequent day and frightened to go to sleep some nights. However, under superficial observation this boy appears "perfectly normal" to our pediatricians here in St. Cloud, being merely a very bright, sensitive and active child. The nightmares the doctors feel are of no significance and will pass with maturity.

Six weeks ago I put ——— on the K-P diet. Within three or four days there was a marked improvement in behavior and sleep patterns. He has experienced two mild nightmares during this period of time and only after stress during the day. The one infraction of the diet (one can of pop administered by the boy's father) produced a very violent nightmare that night with two subsequent days of difficult behavior. When on the diet the boy is much happier and easier to get along with. At age five, sees such a difference in himself that he controls his diet completely when not at home, refusing any food offered to him. Even at home he is reluctant to try new foods worrying that they might make him do "bad things". I am no longer faced with a negative reaction to the majority of requests made of him. He plays much better with other children.

There is no doubt whatsoever in my mind that this child's system cannot tolerance food additives.

However, I need medical confirmation of the above, both for the father's sake and also so that I may present school authorities with some doctor's request that ——— adhere to this diet 100 percent during the coming school year.

Are there any physicians in the Minneapolis-St. Paul area who are familiar with your diet program whom I might contact for an appointment? If not the Minneapolis-St. Paul area, please advise me the name and address of the closest physician. A stamped self-addressed envelope is enclosed for your convenience.

I will daily await your reply.

Thanking you for your cooperation, I remain.

Very truly yours,

——— ———.

SMITHTOWN, N.Y.

DR. B. FEINGOLD,
Kaiser Permanente, Medical Center,
San Francisco, Calif.

DEAR DR. FEINGOLD: So much has happened since I last contacted you that I felt it was quite necessary to write to you once again.

As far as my son is concerned, he is doing extremely well. He is entering a regular first grade class this year and there should not be any problems.

Aside from ———, I did get in touch with Mrs. ——— and she was able to help me quite a bit. Also, I have decided to set up an organization here in Smithtown in order to help other mothers and fathers who have hyperkinetic children. I cannot believe the success I have been having. My pediatrician is cooperating with me and refers his patients on the diet to me so as I can help the mothers. Also, just from word of mouth, so many people have contacted me who are interested in the diet. I have discovered more and more foods which contain nothing artificial and have compiled a list which I pass on to the parents. There are at least five other children on the diet now, and the diet is working for them. At least ten other parents have contacted me and I have explained the diet to them and they are beginning with the diet presently. I have been asked to speak at the schools about the diet, and of course I intend to do so.

Also, CBS TV contacted me two weeks ago and came here for an interview with my son, me, the other mothers who have their children on the diet, and also teachers and psychologists from the schools. Records were brought, and there was no doubt concerning his tremendous progress. They were quite interested in following my meetings and also the progress of the other children.

Of course, there are those parents who feel that the diet is just too much bother, and this is really quite sad. I also find that the pediatricians are quite discouraging in that they remark that everything you eat has artificial chemicals in them, and this really turns the parent off. Also, many parents do not understand the diet and this is quite a problem. I hope that this group of ours can help to solve this problem in the future.

Again, I thank you and Bless You,

——— ———.

OAKLAND, CALIF., *August 19, 1974.*

BENJAMIN FEINGOLD, M.D.,
Kaiser Hospital, 2200 O'Farrell, San Francisco, Calif.

DEAR DR. FEINGOLD: We have a hyperkinetic child and have followed with great interest your comments published in the newspapers and on CBS radio regarding food additives in the form of artificial flavors and colors.

Our son was diagnosed as hyperkinetic and dyslectic at age seven but is now almost thirteen years old and has been on 20 mg of ritalin every three and a half hours day in and day out for all these years. Without medication he has been absolutely impossible to tolerate and completely unable to function at school or at home. I felt that watching his diet so very closely as you suggested would be an added burden that I couldn't take on.

However, last Saturday, August 10, we started a week of various home entertaining, that Saturday being the busiest day of all, with some guests arriving for lunch, staying for dinner with still more guests, and then an evening at the theater. He got his morning medication, and then I was too busy to remember to remind him of additional doses. While sitting in the theater and listening to the mild chatter of the children in our group I suddenly remembered about Chris's lack of ritalin during the whole day, and sat stunned as I realized that he was behaving in a perfectly normal fashion. I quickly ran over the list of foods and beverages served and knew there was nothing artificial in any of my menus. I was so excited that I could hardly wait for the next day! I told him what we were going to do, he agreed to eat no candy or chewing gum, and we had a succession of medication-free days. Thursday I served a giant pepperoni pizza from a delicatessen, and within five minutes was "in orbit." The orbiting lasts far longer than one dose of ritalin can compensate. However I suppose that would depend upon how much of the food additive is ingested.

At any rate, we are thrilled, our pediatrician is thrilled and he is thrilled. He reads labels very carefully now, and has his own stick of butter (the rest of us use margarine). He has always hated taking his medicine and would rather give up phony goodies than take ritalin.

If you have any suggested reading that we can do, or efforts that we can do on your behalf in order to fight the food lobbies, we would be most grateful to hear from you.

We and thousands of other parents of hyperkinetic children will be forever grateful to you for your research. The children themselves will be deeply in your debt.

Sincerely,

———— ————.

DEAR DR. FEINGOLD: To be deeply indebted to someone for a whole year without so much as a thank you is nearly an unpardonable offense: however, my family and I hope you will accept our most sincere gratitude for making the last year the happiest one we have shared.

I am the mother of four daughters, ages 5 months to 4 years. The oldest is (was) hyperkinetic. You have heard harrassed mothers' stories countless times, so I won't go into detail. Suffice it to say that life was miserable for all of us. I lived in horror through each succeeding pregnancy that I might have another child like her.

On December 22, 1973, ABC aired a documentary, "Green Grow the Profits"; and by the grace of God, my parents saw it.

The next morning I heard about your work and immediately stopped her Ritalin and put her on a diet eliminating artificial colors and flavors and preservatives.

In three days there was nothing short of a miraculous transformation. What had been a whining, crying, sullen, disagreeable, restless child who had never slept through the night was suddenly a truly sweet little girl who slept eleven hours at night and took an afternoon nap without argument.

In the first week I cried many times with relief and joy over things like a giggle and the first "OK, Mommy!" that I have ever heard. In ten days she learned all the nursery rhymes in a large book, every story book in the house word for word, several songs, and endless TV commercials.

When it finally became available, we rented the movie from ABC and made it available to our local hospital for inservice education. Several doctors saw it then and were skeptical but interested and want to know more about it.

About three months after she started the diet, our daughter was taken by a neighbor to a pre-school eye screening exam but refused to cover one eye. When the nurse tried to bribe her with candy, she said, "If that has artificial coloring or artificial flavoring, I can't have it. It makes me feel bad."

Yesterday, our first four copies of your book, Why Your Child Is Hyperactive arrived. Two have been given to doctors, one is to lend, and one is our own copy; but I must admit that even my own copy (I read it first) has already been lent to a mother of another hyperkinetic child who heard through our small town grapevine that I might be able to steer her in the direction of some help.

My husband and I plan to donate a copy of the book to each school library in town and also to our public library. This is something that should be shouted from the rooftops!

Because we have had such success so far, we plan to continue to eliminate all preservatives. Food preparation is not a problem for me, and I have reason to believe that she does have an intolerance to at least one preservative.

We have fortunately been able to purchase ice cream (Breyers), frozen baked goods (Sara Lee) and bread (Arnold's Hearthstone white), and flavored yogurt

(Breyers) with all natural ingredients. My sister has even located a German butcher in Chicago who makes sandwich meats without artificial ingredients or preservatives.

I would like to know, please, about sodium saccharine. Is it all right to use?

Dr. Feingold, unless you have lived with hyperkinesis, even you will never know the real magnitude of your work. Thank you is a completely inadequate expression of our feelings. I only wish that we might have been able to help you in your research.

Sincerely,

—— ——.

BALTIMORE, MD., *December 3, 1974*.

BEN F. FEINGOLD, M.D.,
Chief Emeritus, Department of Allergy, Kaiser Permanente Medical Center, San Francisco, Calif.

DEAR DR. FEINGOLD: I am writing to let you know the progress of ______ ______, ______ has changed in many ways to numerous to give you a complete report, however, I will tell you the most dramatic changes.

Needless to say, she is no longer on the drug dexedrine. This was the first thing I stopped. The second thing that was necessary was to have ______ transferred from her class into a new one with a teacher that was not prejudice against her for her previous behavior. This has worked out beautifully. She has adjusted very well to her new class and teacher.

The school was in complete agreement with me as soon as I explained to them what I was trying to do. I had two meetings with ______'s teachers and the school social worker, Ms. ______. Ms. ______ had heard of the Feingold diet but had not heard of it being tried.

I was very surprised that so many people had such a negative attitude about the diet. I had such complete faith in you from the beginning it was very hard for me to believe that people would not be receptive to anything that might stop children like ______ from taking drugs to controlling their behavior. Even ______'s doctor did not truly believe that it would help.

I wish all parents and doctors treating children for hyperkineis could see ______ perhaps then they would be more willing to go to the trouble to find out more about the diet. I myself could not be more pleased about its results in ______ case.

______ can play with other children for days now, where before she would be fighting with them in an hour. She has been put on the safety patrol in school. She brings her homework home everyday and almost enjoys doing it. Before, she would tell me she had none. I can reason with her now and she can see she might be wrong, where before nothing could make her believe the world was not against her. Our home life has changed, we still have loud disagreements but this is normal in every family.

Dr. Feingold, I wish you could see this little girl reading labels on anything and everything before she will eat it. When someone offers her something she will ask what the ingredients are before she will take anything. If they can't tell her she just says, "No Thank You". It is so beautiful to watch her change more and more each day. Now she really cares.

I once thought I was so alone in my fight to get ______ off the drugs that controlled her. Now she can be herself and be proud as I am. Now, I am looking forward to many happy days for my little daughter and I can find no words to say what is in my heart but . . .

Thank you,

—— ——.

DOVER, MASS.

DR. BEN FEINGOLD,
Kaiser-Permanente, Health Care Program, Kaiser Research Institute, San Francisco, Calif.

DEAR DR. FEINGOLD: Thank you so very much for rescuing our son from a tension-frustration pattern which seemed to doom him to a life of failure despite his obvious intelligence and charm. We have followed your K-P diet faithfully for over a month with terrific success—and there have been three goof-offs which prove indisputably that your theories in regard to artificial flavors and colors are entirely correct.

I have had a very fruitful discussion with Boston USFDA people, and they are interested in pursuing the matter further.

Meanwhile, may I ask you a few questions? You suggest that cider vinegar not be used at all. Is this because it derives from apples which are in Group I? If that is so, and if apples prove to be okay, then would cider vinegar be okay too? And then would mayonnaise made with cider vinegar be okay provided it had no artificials? Similarly with wine—is it prohibited because it is made from grapes? If grapes were okay, would natural wines then be okay? And, what is the objection to beer?

I intend to comb the "standards of identity" section of the Federal Government Regulations, and compile a list of foods which don't need to list artificial color/flavor on the label, such as butter, and then to ask particular producers whether or not they do include such colors and/or flavors. Some of our local makers do not, and boast of it. They include Cain's pickles and chips and mayonnaise, Breyer's ice cream. (That reminds me—are pickles out because of cucumbers? Can pickles come back in if cukes are okay? And, is there any objection to pickled beets, cauliflower, watermelon, etc.?)

I have been passing out the enclosed two sheets to parents, doctors, pharmacists who sell Ritalin, etc. Everyone seems genuinely enthusiastic about trying your K-P diet when they realize how simple it really is and how quickly results can be seen—both positive and, after a goof-off, negative. Our town is particularly good at dyslexia and other learning disabilities and I am sure I can get our Ch. 766 Core-evaluation team interested in K-P. That should locate a lot of other kids of all ages who are "hyper-active". Do you want them to send you field data?

Incidentally, pediatricians seem to have heard generally about your diet, but they also seem not particularly anxious to persuade parents to try it! I have heard several times: "Our doctor mentioned artificial colors and flavors but said it wasn't a well-researched theory and said he couldn't be very helpful as to what would be an okay diet, so we didn't do much about it." That is why I have been very aggressively positive in my own pitch for K-P . . . and at the same time I have not exaggerated one bit.

Thanks again for giving us our boy back—the good results were, happily enough, first noticed on my birthday . . . what a terrific present! I hope you will answer my letter, so we can together help a lot of other frustrated kids and parents and families and teachers!

Gratefully yours,

——— ———.

Senator KENNEDY. Our next panel of witnesses consist of Mrs. Otis and her son, Raymond Otis, from Dover, Mass.; Mr. Mike Hathaway and son, David, from the District of Columbia area; Mr. and Mrs. Allan Harbert, from Bridgeton, N.J.; Mrs. Woodruff and son, from Bridgeton, N.J.; Mr. and Mrs. Morrison, from the District of Columbia area; and Mr. Alan Ackerman, from New York City.

And I want to tell Mr. and Mrs. Harbert and Mrs. Woodruff that Senator Williams asked me to extend a warm welcome to you here today. He could not be here. He is addressing a foster grandparents meeting.

While he is unable to be here, he looks forward to reading the testimony.

First of all, I want to extend a warm word of welcome to you. I think you heard during the opening comments what the whole thrust and purpose of this hearing is. I know that you have all had some direct experience with this type of dietary program.

We are interested in exploring the value of the program and determining some of the reactions to it. We will have the Commissioner of the Food and Drug Administration come up afterward and tell us a little bit about the attitude of the Food and Drug Administration. He will also tell us what will be necessary to try to prove some of the early and very hopeful results of the testing program.

We are extremely interested in hearing of your experiences and of your evaluation of this program.

We value very much your personal experience. We hear about a program, we get studies and we read about it, but, too often, we lose the human dimension.

To the extent that it is possible, we would like to try to obtain a sense of what you have been experiencing.

Senator BEALL. Before you start, could I make a brief statement?

Senator KENNEDY. Sure.

STATEMENT OF HON. J. GLENN BEALL, JR., A U.S. SENATOR FROM THE STATE OF MARYLAND

Senator BEALL. I am sorry I was not here prior to the time Dr. Feingold testified.

I want to thank you, at the outset, for scheduling today's hearing on the findings of Dr. Ben F. Feingold with respect to the possible link between hyperkinesis, or hyperactivity, and food additives.

I urged our Health Subcommittee, as part of its drug hearings, on October 30, 1973, to call Dr. Feingold, and the chairman indicated he would do so. Therefore, I am most appreciative for today's hearings.

I ask unanimous consent that my letter to the chairman be printed following my remarks.

Hyperactivity is a problem, which appears to be growing, affecting millions of schoolchildren.

For example, the California Association for the Neurological Handicapped estimated, from 1961 to 1973, the instances of hyperactivity among schoolchildren in California rose from 2 percent to an average of 20 to 25 percent and, in some cases, 40 percent of a school's population. Many of these children are bright and should be performing well. Often, however, they have learning difficulties and behavioral problems.

Dr. Feingold, by altering the diet of hyperactive children, achieved dramatic results in terms of improved behavior of such children. Significantly he was able to trigger a return to hyperactivity, sometimes in a matter of hours, by putting artificial substances back into the diet.

I first learned of Dr. Feingold's work approximately 2½ years ago. Dr. Feingold, after reading about legislation I authored to attack the Nation's reading problem, wrote me about hyperactive children and his findings, and pointed out that hyperactive children often experience reading and learning difficulties.

In October 1973 I made a floor statement calling Dr. Feingold's findings to the attention of my colleagues and the country.

Since that initial contact, I have followed Dr. Feingold's progress and have endeavored to interest the Federal Government in following up on his dramatic results. This effort included numerous correspondences and contacts with the Food and Drug Administration, the National Institutes of Health, the National Institute of Mental Health, and the National Institute of Education.

Dissatisfied with the Food and Drug Administration's responses, I invited them to my office. Their reaction was skeptical and negative. They refused to lend any support.

In February of this year Food and Drug finally shifted positions and indicated an interest in Dr. Feingold's contentions. I placed the New York Times story reporting on this shift into the February 27 Congressional Record.

Fortunately, Mr. Chairman, one of our newest agencies, the National Institute of Education, NIE, which in the past has been the subject of much congressional criticism, was receptive earlier and, with my support and endorsement, authorized a followup study of the Feingold findings. I certainly want to congratulate NIE for its willingness to support what others at HEW at the time seemed to look down upon.

On June 6, 1974, I announced in the Congressional Record that NIE has awarded a $60,000 grant to Dr. C. Keith Conners, of the University of Pittsburgh, to test the Feingold hypothesis.

Dr. Conners' study was completed recently, and it concluded that the Feingold diet "may reduce hyperkinetic symptoms."

The Conners' study, although supportive of Dr. Feingold's research, is by no means the final answer. Many questions remain unanswered.

But, if Dr. Feingold is right, then many of the millions of hyperactive children, many of whom are being treated by drugs, can be helped with an alteration of their diet.

Many questions remain unanswered, but can the reluctant HEW agencies contend any longer that Dr. Feingold's thesis does not justify a major research undertaking on this complex phenomenon of food additives and hyperactivity? I think not.

As I stated in my 1973 letter to the chairman requesting this hearing:

> Since early May I have been communicating with Dr. Feingold and the Food and Drug Administration and the National Institute of Mental Health in an effort to call attention to his findings and generate additional support for his efforts. At the present time, many hyperactive children are being treated with powerful drugs. If hyperkinesis can be controlled simply by changing children's diets, then we certainly should find it preferable to move in this direction. Furthermore, if there is a link between those artificial food additives and hyperkinesis, then the entire use of artificial colors, flavors, and other additives should be examined with regard to their potentially dangerous effects on humans.
>
> I am hopeful that, as a result of today's hearings, HEW, with the exception of NIE which has been responsive, will get off the dime and conduct a major research effort in this area.

[The documents submitted by Senator Beall for the record follow:]

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United States Senate
COMMITTEE ON
LABOR AND PUBLIC WELFARE
WASHINGTON, D.C. 20510

October 30, 1973

The Honorable Edward M. Kennedy, Chairman
Subcommittee on Health
Senate Labor and Public Welfare Committee
4220 Dirksen Office Building
Washington, D. C.

Dear Ted:

I urge that one of the earliest witnesses during the upcoming hearings on drugs be Dr. Ben F. Feingold, Chief-Emeritus, Department of Allergy of the Kaiser Foundation Hospitals and Permanente Medical Group.

Dr. Feingold has found that artificial food substances may be a cause of hyperkinesis, of hyperactivity, in children. Hyperkinesis is a major problem in the country. A conservative estimate is that moderate and severe disorders are found in about 3% of elementary school children; however, this varies from community to community. For example, it is estimated that the instances of hyperkinesis among school children in South San Francisco is a conservative 5% and it is as high as 25% in Monroe County in upstate New York. The California Association for Neurological Handicapped estimates that in the past ten to twelve years instances of hyperkinesis among California school children has risen from 2% to an average of 20 to 25%, and in some cases 40% of the entire school population.

A significant number of the children with hyperkinesis have special learning or reading disorders also. Dr. Feingold's research indicates a link between hyperactivity in children and artificial food coloring and flavoring.

For example, in one group of twenty-five hyperactive children, Dr. Feingold was able to eliminate or dramatically reduce the disorders for at least fifteen children by putting them on a diet that was free of artificial food flavors and colors. Even more dramatic was the ability to trigger the return of hyperkinesis, sometimes in a matter of hours, by putting artificial substances back into the child's diet.

Since early May I have been communicating with Dr. Feingold and with the Food and Drug Administration and the National Institute of Mental Health, in an effort to call attention to his findings and generate additional support for his efforts. At the present time many hyperactive children are being treated with powerful drugs. If hyperkinesis can be controled simply by changing childrens' diets, then we certainly should find it preferable to move in this direction. Furthermore, if there is a link between those artificial food additives and hyperkinesis, then the entire use of artificial colors, flavors and other additives should be examined with regard to their potentially dangerous effects on humans.

Therefore, I strongly urge that the Committee give Dr. Feingold an opportunity to present his findings. I appreciate your cooperation.

With best wishes, I am

Sincerely yours,

J. Glenn Beall, Jr.

JGB/jas

[From the Washington Post, Monday, Oct. 29, 1973]

Study Links Food Additives To Hyperactivity in Children

By Morton Mintz

Washington Post Staff Writer

A medical specialist says that artificial colors and flavors in foods and beverages may be an important cause of a serious behavior disorder believed to afflict millions of school children.

He bases his theory on experiments in which afflicted children come to behave normally when put on a diet free of synthetic colors and flavors, only to revert to their maladjusted condition when they violate the diet by so much as a bite.

The specialist is Dr. Ben Feingold of San Francisco. He is chief emeritus of the Department of Allergy of the Kaiser Foundation Hospitals and Permanente Medical Group.

The disorder, called hyperkinesis or hyperactivity, interferes with a child's attention span—leading to reading, spelling and other learning difficulties—and is reflected in disruptive and even compulsively aggressive behavior.

The disorder occurs almost exclusively in boys. Usually only one child in a family is affected.

Hyperkinetic children generally—but not always—are genetically predisposed to allergies. Usually they have normal or high IQs. And, says Feingold, they ingest substantial amounts of chemical colors and flavors, as shown by diet diaries.

Frequently, physicians prescribe for hyperkinetic children drugs that in adults are stimulants. The drugs are amphetamines and Ritalin, the trade name of the CIBA-Geigy Corp. for methylphenidate hydrochloride.

Feingold has found, that sharp increases in the disorder and in learning difficulties over the last 10 years have occurred in parallel with increases in the dollar value of the production of artificial flavors and soft drinks.

There are 2,500 to 3,000 flavors—some of them secret chemical formulations—but only 11 basic synthetic colors, Feingold says.

The colors and flavors constitute about 80 per cent of all food additives. They proliferate in "convenience" foods and products such as soft-drink powders, the physician says.

Feingold reported initial findings to an American Medical Association meeting in New York City in June and at an international food symposium in London in September. He said in a phone interview with The Washington Post that he is now preparing an article for the British Medical Journal, published by the British Medical Association.

At the time of the AMA meeting, Feingold said, he had achieved "dramatic. results" with the special diet in 15 to 18 of 25 hyperkinetic children in his practice. Some of the children who did not

See ADDITIVE, A9

Hyperactivity in Children Linked to Food Additives

ADDITIVE, From A1

did not stick to the diet, he said.

Currently, the allergist told a reporter, he has successfully treated more than 50 children. In addition, he said, other physicians independently have duplicated his results.

Feingold emphasized that the special diet doesn't always work, because there are actually [illegible] [illegible] [illegible] of [illegible] [illegible]. Sometimes it works [illegible] patients with [illegible] [illegible] [illegible] [illegible]ures, he said.

Feingold told of a 7-year-old boy who had been hyperkinetic during much of his life. No therapy worked. But after a few weeks on the special diet the boy became well adjusted at home as well as at school.

The physician said that even a slight violation of the diet can cause symptoms of hyperkinesis to emerge within a few hours and to persist for 24 to 48 hours.

"In view of our ability to relate this behavioral disturbance in children to food additives in turning on and turning off these adverse clinical responses," Feingold told fellow allergists at the AMA meeting, "we raise the following question:

"Is it possible to attribute the increase in hyperkinesis and learning difficulty . . . to the increased consumption of these chemicals in our foodstuffs?"

Feingold told of a California study indicating that in the last 10 years the incidence of hyperkinesis in certain school populations increased from an average of 2 per cent to 20 to 25 per cent and, in some cases, to 40 per cent. He said no correlation has been shown between rates of affliction and socio-economic factors.

The dominant occurrence of hyperkinesis in boys and its absence among a victim's brothers and sisters may offer clues for researchers, but "we really do not know" the explanation, Feingold said.

"Do the additives ingested by the mother during pregnancy affect the unborn child?" the allergist wonders.

He points out that additives, like drugs, can cross the placental barrier to the fetus and affect its development. It is at least conceivable, he says, that increased consumption of food additives by pregnant women could be an "important factor" in conditioning a fetus to react to additives in childhood with hyperkinesis.

An average child's breakfast today may include foods "loaded" with enticing flavors and colors, including cereals, beverages, pancakes made from a mix and frozen waffles tinted by a chemical called tartazine, Feingold said.

A "conscientious and concerned" mother may give her child chewable vitamins. These, too, contain chemicals.

The child goes off to school where, at lunch, he gets more flavorings and colorings in hot dogs, luncheon meats, ice cream and beverages other than milk.

"Is it any wonder that our children are jumping and failing to learn?" Feingold asked at the AMA session.

The conscientious mother, or school authorities, may try to cope with the possibly chemically created disorder by dosing the child with more chemicals—an amphetamine or Ritalin. These drugs, too, are dyed, Feingold said. Some children also are given strong tranquilizers that, again, are artificially colored.

How many children get the amphetamines and Ritalin, which CIBA-Geigy has heavily promoted for hyperkinesis, is unclear.

The number estimated in 1971 by the National Institute of Mental Health was up to 200,000. The current estimate made by CIBA-Geigy for Ritalin alone is 250,000.

A company spokesman said Friday that the firm was trying to clarify the figures in the light of testimony given at a Senate hearing in July, 1971, by CIBA-Geigy president Thomas O. Boucher.

He said that the firm in 1970 sold 243 million Ritalin tablets, that some 2 million persons too kthe drug, and that "its use for hyperkinesis is approaching 30 per cent . . . of production." In the same year, Ritalin accounted for $11 million in sales, or 15 per cent of the firm's total.

Feingold's research associates were Drs. Donald F. German, Alice Friedman, Richard Braham and Ellamae Simmons.

In a related development at Georgetown University, researchers have reported on a laboratory study of some food additives used to prevent spoilage of beverages and canned and frozen foods by disease-producing bacteria.

The additives act as strongly against animal and human cells as against the germs, the study indicates.

Further investigation is necessary, "but present evidence would urge caution in eating large quantities of food containing such additives," said microbiologist Thazepadath Sreevalsan.

The Georgetown study, done in collaboration with the National Institutes of Health, involved tissue cultures in which additives were shown to inhibit the growth of cells, to alter their shape, and in some cases to destroy them.

The results, reported in the Proceedings of the National Academy of Science in August, also showed that the chemicals did not act selectively merely against the bacteria that cause spoilage, but were at the same time anti-cell agents.

"There may be a mechanism whereby the stomach tissue in a whole organism is able to detoxify the compounds in humans, but even in that case, ingesting too much might overload the mechanism and still pose a danger," said Associate Prof. Sreevalsan.

He said that most anti-bacterial food additives are fatty acids that, in the concentrations in which they are used to prevent spoilage, have not exhibited "any gross animal or human toxicity."

All human cells in the study are inhabited by these compounds as well as by nitrite. For that reason, "the large consumption of foods containing the compounds "may potentially interfere with the function of some human cells," Sreevalsan said. The same would apply to drugs such as salicylates—aspirin, for example—that also are fatty acids, he said.

The study was done with cells from human livers and intestines and with chicken embryo cells grown in laboratory tissue cultures.

Sreevalsan's co-researchers were Eliot Ginsburg, Daniela Salomon, and Dr. Ernest Freese.

Wash. Post
1/13/74

Study to Test Effects Of Food Additives

By Thomas Grubisich

Washington Post Staff Writer

A BOSTON psychologist has been awarded a $50,000 federal grant to test a controversial claim that artificial flavors and colors can cause hyperactivity.

Dr. C. Keith Conners, director of the Human Resource Institute of Boston and an associate professor of psychology at Harvard University, said "we should have results in six months."

If the study validates the claims of Dr. Ben F. Feingold that artificial additives can trigger the symptoms of hyperactivity, it would, Conners said, "have revolutionary effects on the food industry and the drug industry."

The food industry would be hard hit because many foods contain artificial additives. The drug industry would feel an impact because drugs are often prescribed for hyperactivity, an increasingly diagnosed behavioral disorder affecting young children.

Artificial additives are a proportionately small but major ingredient in most foods commonly eaten by children—cereals, various snacks and desserts, and beverages. The additives are used extensively by the food industry because they have reduced reliance on natural foods, like some fruits, that are expensive and not widely available.

After Feingold's claims were published last year, they were attacked by the Grocery Manufacturers of America, Inc., which represents big food companies. The GMA critique said flatly: "We know of no data which relate behavioral disturbances directly to the ingestion of food additives." It said Feingold's study was unscientific and subjective.

Though the GMA has not, so far, made any comment on the design of the Conners study, its criteria for any new investigation call for more elaborate controls.

The GMA criteria call for four diet groups to be studied—one with no synthetic colors and flavors, a second with another dietary modification, a third with no modification but clinical monitoring and a fourth with no modification but given a placebo drug.

Conners said in an interview "I don't see how the third group would aid the study, and as for the fourth group, it would be interesting, but I don't know that we need it at this point. You can't answer all questions in one study."

Conners will study two groups—one on an additive-free diet and another on a diet with another restriction. They will switch diets after a month.

The GMA proposal also called for a study lasting a year or more. Conners, whose study will last two months, said a longer one would be "unrealistic" because children will be withdrawn from all drugs during the test period.

Food and Drug Administration officials have sought additional assurances from Conners that dietary restrictions will be rigidly imposed. Conners noted that half the 100 children to be studied are in institutions, where dietary controls will be easier to impose than with the others, who are outpatients.

TUESDAY, NOVEMBER 13, 1973

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Seeking Facts About Additives

In calling for a Senate investigation of the effect of artificial additives on children's health, Sen. J. Glenn Beall Jr. (R-Md.) has taken a needed and potentially important step. Over the past few years, large numbers of parents have been concerned, even alarmed, about foods their children eat that are laced with additives. Laymen cannot be expected to have a sophisticated knowledge of the several thousand additives intentionally put into today's foods, nor should they be expected to take it on faith that food companies use only safe additives. It is true that large numbers of additives are safe and highly useful. Nevertheless, the public's health is involved and each additive needs close scrutiny of both its potential benefit or danger.

The need is for information that adds light to the subject, not heat. As nutritionist Jean Mayer has noted, opposing factions on additives often become shrill: "Enemies of additives give us a nightmarish vision of a food industry dominated by a few malevolent men of great wealth who in their craze for profit are indiscriminantly spraying their products with poisonous chemicals. By contrast, the Bull Mooses of industry have perceived any criticism of additives as an attack on Science, Technology, the American Way of Life and Western Civilization."

As a member of the Senate Health Subcommittee, Sen. Beall's interest in additives was aroused by the findings of a California physician who believes artificial additives may be a cause of hyperactivity in children. At the moment, such a finding lacks the validity that proceeds from large-scale scientific testing. But neither can it be dismissed merely because the California survey was small. This is why the investigation proposed by Sen. Beall is potentially important.

Daily Record
November 7, 1973

Washington Report

By SENATOR J. GLENN BEALL, JR.

Food Additives

American children are probably the healthiest and best cared for boys and girls in the world. Medical research has conquered childhood diseases such as polio, and we have improved the nutrition of many youngsters by providing milk and balanced meals through the federally assisted school lunch program.

Our children are growing up to be taller, stronger and healthier than any previous generation of Americans, but we have not solved all of our youngsters' health problems.

New medications and therapy are constantly being developed, and earlier this year I became aware of the work of a West Coast doctor who is moving in a different direction.

Dr. Ben F. Feingold of San Francisco wrote to me about a bill I introduced to improve the teaching of reading in our schools. He said that reading problems may be related to a disorder called hyperkinesis, or hyperactivity, in children, because it can effect a child's ability to concentrate.

The interesting thing about Dr. Feingold's work is that he was able to eliminate the disorder, or dramatically reduce it, simply by putting children on a special diet rather than prescribing a variety of potent drugs.

The startling thing about the diet is that there is nothing special about it—except that it is free of all artificial food flavoring, coloring and additives.

As a member of the Senate Health Subcommittee, this has impressed me as a potential discovery of great importance. I have therefore asked that Dr. Feingold be invited to testify about his work when the subcommittee meets for hearings later this month.

Hyperkinesis has been affecting an increasing number of our children. One study found that its incidence among school children has risen from about 2 per cent to more than 20 per cent over the past 12 years.

If it is possible that there is a link between this condition and the presence of artificial food additives, then it would appear that Dr. Feingold has not just found a cure. He may have found a major cause of the disorder and a reason for its increasing presence among our children.

The Health Subcommittee will be looking into these questions as we go forth with our hearings in mid-November. It may also be advisable to conduct a broader investigation supported by a federal research grant.

If this link is found to exist, then we would be in a position to do several things.

First, we would be able to treat hyperactivity in many cases without resorting to powerful, and perhaps dangerous drugs.

Looking further into the situation, we might perhaps want to examine the entire question of artificial colorings, flavors and other food additives with regard to their potentially dangerous effects on humans.

"Washington Post" October 31, 1973

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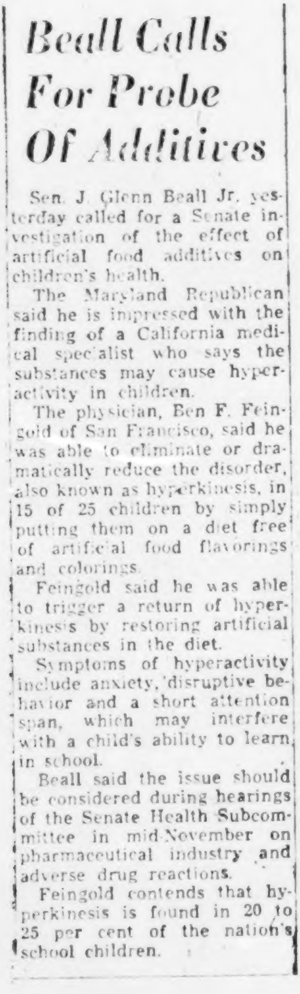

Beall Calls For Probe Of Additives

Sen. J. Glenn Beall Jr. yesterday called for a Senate investigation of the effect of artificial food additives on children's health.

The Maryland Republican said he is impressed with the finding of a California medical specialist who says the substances may cause hyperactivity in children.

The physician, Ben F. Feingold of San Francisco, said he was able to eliminate or dramatically reduce the disorder, also known as hyperkinesis, in 15 of 25 children by simply putting them on a diet free of artificial food flavorings and colorings.

Feingold said he was able to trigger a return of hyperkinesis by restoring artificial substances in the diet.

Symptoms of hyperactivity include anxiety, disruptive behavior and a short attention span, which may interfere with a child's ability to learn in school.

Beall said the issue should be considered during hearings of the Senate Health Subcommittee in mid-November on pharmaceutical industry and adverse drug reactions.

Feingold contends that hyperkinesis is found in 20 to 25 per cent of the nation's school children.

Baltimore Sun

October 31, 1973

Probe of food additives asked by Beall

Washington Bureau of The Sun

Washington — Senator J Glenn Beall, Jr. (R., Md.) asked yesterday for an investigation of artificial food additives and their possible contribution to health and learning problems among children.

Senator Beall, a member of the Senate Health Subcommittee, urged that the subject be included in its hearings next month on the pharmaceutical industry and drug reactions.

The possible link between childhood problems and artificial food colorings and flavors, according to Senator Beall, was detected by a San Francisco medical specialist, Dr. Ben F. Feingold.

Dr. Feingold, the senator said in a press release, was able to eliminate or dramatically reduce hyperactivity in 15 of 25 children by simply removing additives from their diet.

"Even more dramatic," the statement said, was the return to hyperactivity when the artificial substances were put back into the diet.

The subcommittee's hearings were scheduled by its chairman, Senator Edward M. Kennedy (D., Mass.), after hearings on human experimentation produced testimony that adverse drug reactions may account for as many as 30,000 deaths a year. A committee spokesman said later yesterday that Dr. Feingold will be called as a witness.

Senator KENNEDY. Thank you, Senator Beall.

We acknowledge both your interest and your leadership in this area. We welcome it and join with you in supporting the steps that will be taken by the FDA, HEW, or another agency to prove these observations and to substantiate early conclusions.

I want to tell the children that we are glad to have them here today. I do not know whether they are missing school. We do not know whether they want the hearing to be long or short.

Maybe you can tell us in your own words when you found out that your child was hyperactive, Mrs. Otis.

STATEMENT OF MRS. OTIS AND SON, RAYMOND ELLIS OTIS, FROM DOVER, MASS.; MIKE HATHAWAY AND SON, DAVID, FROM THE DISTRICT OF COLUMBIA; MR. AND MRS. ALLEN HARBART, FROM BRIDGETON, N.J.; MRS. WOODRUFF AND SON, FROM BRIDGETON, N.J.; MR. AND MRS. MORRISON FROM THE DISTRICT OF COLUMBIA; AND ALLEN ACKERMAN, FROM NEW YORK CITY, A PANEL

Mrs. OTIS. I never did. That is one of the fascinating problems to me.

We have been told we are allergic. We have covers on our mattresses. We have been told we are a little screwballed, and we were sent to a psychiatrist for 2 years. We have been told we had dyslexia so we had special tutors. We have been told all different kinds of things and that is not the case at all.

The medical professions have not been given the word about Dr. Feingold strongly enough to encourage them to encourage parents to undertake what looks like a fairly startling change in family habits. It turns out not to be a problem at all.

I have written a list of what our family now eats. If you would like to know what you can have with your nieces and nephews, you might like to.

We take our lunch to school. It is very simple.

Mrs. Feingold's recipes are very, very good.

Raymond, you may notice, is a bit twitchy today as a result of, on Monday, I forgot to make sure he had his packed lunch, and he took the public school hot lunch. The ravioli was all right. The tomato sauce was all right. The corn was all right but there was butter on the corn. In the butter there is color.

So, for 3 days, he will be fidgety. He will be fine tomorrow.

Senator KENNEDY. During the period you outlined, did any of the medical professionals that you saw ever prescribe any drugs?

Mrs. OTIS. Yes. We used Ritalin for a year and a half. Raymond is very smart. Inside of his own head, he realized it was not doing him real good. It was making him quiet and dopey. He asked if he could stop taking it.

I think he is a better doctor than most, so I said sure. It is about 6 weeks after that that we started the Feingold regime. Interestingly, the physical aspects, the way his eyes are, the way his general feeling of good health, and calmness and cheerfulness and happiness with himself, which was fairly obvious when he started taking Ritalin, was about 40 times as obvious within 3 days of when we started Dr. Feingold's diet. It is really startling.

Senator Kennedy. How did you find out about Dr. Feingold's diet?

Mrs. Otis. We went to summer school this year and Ray's English coach strongly suggested that we do it.

Senator Beall. Where was that?

Mrs. Otis. A school for dyslexic children, Carroll School in Lincoln, Mass.

Senator Kennedy. Did you just start on your own?

Mrs. Otis. Certainly.

Senator Kennedy. Maybe you could tell me a little bit about the changes.

Mrs. Otis. When Raymond wakes up in the morning, his hair is not all scrubbed up in back and he does not grind his teeth any more.

You can ask a question and get a paragraph of an answer. He can concentrate beautifully.

In going to the school, we have had the opportunity of being alone in the car 3 hours a day. So I was looking at him pretty carefully when I was not watching traffic.

When we started out, he could work with—maybe get an inch of weaving done—but by the end of the summer, he was making these things 4 and 5 feet long and completed. He started it at the beginning and went to completion of the project, which is a great help when you have to go to school.

Senator Kennedy. This, you attribute to the change in the diet?

Mrs. Otis. Entirely. He has become a terrific mountain climber. He has not done anything dumb.

You were asking Dr. Feingold if the additives were dangerous. I would like to make a point that they are terribly dangerous because they can lead to foolish, sometimes nearly suicidal behavior on the part of these children.

I know a boy whose hobby is lying down in the middle of the road to see how long he can wait before a car comes. He is 6.

I know boys that lose their temper and throw large rocks at their sisters. That is dangerous behavior.

So I think that the additives have got to be classified as very dangerous, indeed.

Senator Beall. How immediate was the reaction of the change in behavior after you started using it?

Mrs. Otis. Three days.

Senator Beall. Three days?

Mrs. Otis. Yes.

I was, as his mother, in very close contact with him and certain we were on the right track in 2 days. Other people began noticing it in 3 days.

The negative reaction, as Dr. Feingold says, comes right back in about 2 hours.

Senator Beall. When he breaks the diet, how immediate is the change in behavior again?

Mrs. Otis. Two or three hours later, I will know something has happened. I will prepare myself to be extremely patient for 3 additional days.

Senator Kennedy. Mr. Hathaway, could you tell us a little bit about your experience?

Mr. HATHAWAY. I have never met Mrs. Otis before, but some of the terms she used sounded so familiar.

We went through a period of about 2 or 3 years where we were told things like dyslexia, special tutoring.

But, after all the testing, the answer that we really came out with, that David was not just a normal child, but above average child, but that did not cure the behavioral problem in school.

He was on the point one time of being removed from school. This year, he is going to be a patrol officer in school as an example of behavior improvement.

We had finally reached a point where we were considering drugs, which we did not want, of course.

When I read an article by Marion Burrows on Dr. Feingold's work, I called Dr. Feingold and talked and discussed with my wife, and then we decided that we will try anything.

We tried it. The results were so good that we could not believe them.

We felt there had to be something more to it.

Within 2 weeks, we saw a definite change in his behavior. Since being a small child, he has been restless, often withdrawn, often hostile. His behavior had reached the point where there was really no reward or punishment that could be offered to influence.

Then we realized that really the unhappiest person with this was not his teacher or us, but himself.

Within 2 weeks, we saw definite change in his behavior. And within a month, he was a different child. He was happy, confident, relaxed. He had manual dexterity which he did not have before. His teachers could not believe it.

We had one incident. I remember he came home from school very unhappy, very withdrawn and hostile. We just said, well, even normal children without allergies to colors or food additives have that, but it continued on the next morning and the next day.

We questioned him about his diet and had he gone off of it. He insisted he had not. He finally confessed he had a carton of chocolate milk at school.

I think, since that time, there have been no infractions that we are aware of. The results have been incredible. There are still problems occasionally, but an increase in school work, an increase in improvement in behavior is so obvious that it is unquestionable.

Senator KENNEDY. Senator Beall.

Senator BEALL. At what date did you do all of this?

When did you become aware of the Feingold method?

You say you heard about it from Marion Burrows. When was this?

Mr. HATHAWAY. This was last fall, about August of 1974.

Senator BEALL. You have had almost a year's experience now?

Mr. HATHAWAY. We actually began about October 1, and found out, surprisingly, that it was not anywhere near as much a problem as it would appear. It takes awhile to get accustomed to the foods. There are quite a few things you can make. It is really not an inconvenience or problem.

We have been on it about a year now.

Senator BEALL. How old is David?

Mr. HATHAWAY. Eleven.

Senator KENNEDY. Do you mind the diet, David?

David Hathaway. No; I do not. It helps me with my work and things. I like it. I am glad to stay on it.

Senator Kennedy. Is the food about as good?

David Hathaway. Yes.

Senator Kennedy. Is there anything you miss, anything kind of special?

David Hathaway. No; after I got used to the diet, I stuck with it.

Senator Kennedy. Do you feel that it made much difference with you.

Are you feeling better these days than you were before, as a result of it?

David Hathaway. Yes; a lot.

Senator Kennedy. You noticed a difference once you started on the diet?

David Hathaway. Before I was on the diet, I could not build models very good. Now, I can paint them and build them good.

Senator Kennedy. What is your favorite model?

David Hathaway. Airplanes.

Senator Kennedy. My son likes those, too. They are tough to do.

Mr. Harbart.

Mr. Harbart. Senator Kennedy, we had a prepared brief statement. I know you asked for this in our own words, but there were several points we wanted to make in our presentation so would you have any objection to my reading it?

Senator Kennedy. No.

Mr. Harbart. This statement is being presented to your subcommittee in an effort to indicate and set forth background of one individual problem relating to hyperactivity.

Our daughter Marian was a hyperactive child. Her symptoms included a failure to sleep at night; inability to concentrate for any length of time; an inability to be pleased by anything that was done for her; poor hearing; poor coordination; restlessness, even during the day; an inability to tolerate failure or frustration; and an inability to leave things alone.

It should be stated that, as a result of the symptoms aforesaid, Marion was not a happy child nor was her younger sister. And, in fact, we were often troubled as a result of her condition.

For example, during the first 3½ years of her life, Marian never slept through the night and was often awake 3 to 4 hours. There were many times when Marian would be unhappy even when offered trips to the local zoo, normal childhood treats, or the opportunity to play with other children.

She also manifested aggressive tendencies, particularly toward her younger sister and even her mother. If she was unable to accomplish anything, she immediately began crying and fussing and could not be placated.

She was unable to watch a television program for any longer than 5 minutes.

She was constantly falling down for no reason at all and had many black and blue marks, scratches, and the like.

When she was 2 years old, while attempting to remove the spool from her mother's sewing machine, the chair on which she was standing slipped from under her, and she fell to the floor, pulling the sewing machine over on her in such a manner to cause a deep gash in her forehead, which required 22 stitches.

On another occasion, her mother was attempting to quiet her so she would go to sleep, but she waved her arms wildly and scratched the cornea of her eyes. To emphasize her problem with sleep, it was determined that, on one occasion, she turned over in her bed 110 times in the course of one-half hour while attempting to go to sleep.

These are just a few examples of the problems Marian faced during the first 3½ years of her life.

When Marian was 3 years old, her mother determined that there was a strong possibility that she was hyperactive. This conclusion became apparent when our second child was born, and the symptoms that Marian had shown were not evident with our second daughter.

As a result, Marian was taken to a local physician who prescribed Ritalin for her. When she was given this medication, her behavior problems seemed to be moderated but it caused, in turn, a severe loss of appetite and a weight loss of 7 of her 37 pounds.

Under these circumstances, the medication was stopped after a period of approximately 7 months. At this point, we determined that she could not sustain any further weight loss and elected to take her off Ritalin.

By fortunate circumstances, 2 days later, her grandfather was watching an American Broadcasting program entitled, "Green Grows the Profits," relating to efforts by the food industry to enhance natural products through the use of artificial colors and flavors.

On this program, Dr. Ben Feingold appeared and set forth the hypothesis that hyperactivity in children was caused by a sensitivity to artificial colors and flavors ingested. Marian's grandfather immediately reported to us that he had seen Dr. Feingold on the program and what Dr. Feingold had said.

Because of the problems we had had with Marian, we decided immediately to remove artificial colors and flavors from her diet.

Within 3 days after she was placed on this food program, we saw a radical change in her personality. In fact, for the first time in her life, she slept 11 consecutive hours. In 3 days, there was nothing short of a miraculous transformation. What had been a whining, crying, sullen, disagreeable, restless child who had never slept through a night was suddenly a truly sweet little girl.

We heard her first giggle and her first "OK, Mommy."

In 10 days, she knew all the nursery rhymes in a large book, knew every story book in the house word for word, could recite countless TV commercials, and sat all the way through Sesame Street for the first time.

Marion started school this year, and we have every reason to believe that she will be truly successful with absolutely no learning disability. We are certain that this transformation came about only because of the work of Dr. Feingold and only hope that other parents with similar problems can be helped as we have been.

Because of our desire to assist other parents and their children, an organization has been formed in our hometown of Bridgeton, N.J., for this purpose. There are approximately 50 children and their parents who have been helped by the food program promoted by this organization.

It should be remembered that this is one little town of 20,000 people, and we have had this type of response in 3 months.

The organization attempts, through publicity, personal consultation and dissemination of literature, to encourage the use of this diet.

Attached hereto as an exhibit are the materials furnished to parents. We also recommend as a first step that parents read Dr. Feingold's book, "Why Your Child is Hyperactive."

[The material referred to follows:]

K-P DIET FOR HYPERACTIVES

(Brands available in Bridgeton Area)

Beverages.—7-Up and Sprite; Nestea regular and lemon; Dole Pineapple Juice; Apple Juice; Welch's frozen or bottle grape juice; Orange or Grapefruit Juice; Cranberry or Cranapple Juice; Tomato Juice; Pear Nectar. All juices can be frozen for popsicles.

Breads.—Arnold Hearthstone Bread; Any white bread and rolls except egg bread (check labels); Arnold Blueberry Muffins; Thomas' Corn Toast-r-Cakes and Thomas' English Muffins. Terrigno's Italian Bread. Make your own French Toast, pancakes, and waffles for breakfast.

Cakes and cookies.—Pepperidge Farm cookies, Goldfish crackers, cakes and pretzels; Sara Lee Products (except Devil's Food cakes); Chock Full O'Nuts cakes; Archway Aunt Mary's sugar cookies, Sugared Molasses and Old Fashioned Molasses (check others); Tastykake Jelly Krimpets and Tastykake Pies (check labels); Nabisco Peanut Cream Patties; Sunshine Vanilla Wafers, Nabisco Fancy Dip Grahams; Ivan's Spiced Wafers; Archway Gingerbread Cookies.

Candies.—Baker's Sweet German Chocolate; Reese's Peanut Butter Cups; Mary Janes; Peppermint, Spearmint, and Crystomint Lifesavers; Wrigley's Spearmint and Doublemint Gum; Bit-o-Honey Bars; Callard & Bowser Butterscotch, Treacle Brittle and Mint Toffee; Tic-Tac (White only).

Cereals.—Puffed Wheat and Puffed Rice; Post Grapenuts, Sugar Crisp and Rice Krinkles; 100% Natural Cereals; Cream of Rice.

Condiments.—Hollywood Health Food Mayonnaise; Mrs. Schlorer's Mayonnaise; Hellman's Mayonnaise; Ritter Green Tomato Relish and Catsup; Heinz Catsup; Haddon House Pickles and Relish; Pure Vanilla Extract; Lea and Perrins Worchestershire Sauce; Cinnamon Sugar for Toast.

Desserts.—Breyer's Ice Cream and Yogurt; Hershey's Ice Cream; Dannon Yogurt; Homemade Rice Pudding, Custard, Bread Pudding. Any home-made pudding (no packaged); no Jello except that made with plain gelatin and fruit juice.

Dairy products.—Butter or Sweet Butter—no Margarine. White Cheese (sharp, Swiss, American, etc.)—check labels; natural yogurt, eggs.

Jams and jellies and syrups.—Smucker's syrups, jellies and jams; Roadside Natural Jams and Jellies (Acme or Pantry Pride). Check labels on other brands for natural content.) Pure Maple Syrup.

Meats, poultry and fish.—Frozen Weaver's Batter Dipped Chicken, Chicken Turnovers; Meyers Chicken and Noodles au Gratin; Natural Turkey Loaf (Acme and DeMaio's) Dietz and Watson German Bologna. Hot Dogs (available at Levenson's, Beder's Better Beef and Dunderback's in Cherry Hill Mall); Oscar Meyer Bacon; Hormel and Morrell canned hams (no flavored ham, bacon, hot dogs or lunch meats); Taylor Pork Roll. Any fresh meat, chicken, fish, beef, pork, etc.; canned tuna fish.

Snacks.—Keebler's Cinnamon Crisp or Milk Lunch Biscuits; Ritz Crackers; Saltines; Wise, Herrs or Valley Maid Potato Chips; pretzels (check labels); Cracker Jacks; Peanut in the shells and other uncolored and unflavored nuts; white popcorn; Ideal Chocolate Fudge Bars (like Fudge-sicles).

Soups.—Campbell's Chicken Rice, Chicken Noodle O's, Curley Noodle, Chicken & Stars, Tomato and Vegetarian Vegetable (always check labels). Home-made soups are best to eat.

Other canned foods.—Franco-American Spaghetti O's with Little Meatballs, Spaghetti with Little Meatballs, Plain Spaghetti; Heinz Macaroni; Campbell's Home Style Baked Beans; Ragu Spaghetti Sauce and Cooking Sauce; any canned vegetables which have no artificial coloring or flavoring.

Vegetables and fruits.—Any frozen vegetables which do not have artificial coloring or flavoring (frozen corn niblets have carotene coloring)—canned niblets do not; French Fries (check labels); any canned fruit which do not have red cherries and are packed in natural syrup.

Other products.—Any noodles, macaroni, spaghetti, etc. which does not have artificial coloring—A. & P., Ronzoni are O.K. Big John's Pizza; Buitoni Pizza and Frozen Ravioli; Celentano Frozen Ravioli, Shells and Lasagna (available at Levenson's)—use home-made sauce; most peanut butters except Jif.

Miscellaneous.—Natural Brand Toothpaste (from General Nutrition Center at Cumberland Mall); Silence is Golden Cough Syrup and Cough Drops; Wesson Oil; Peanut Oil; A & P Pure Corn Oil. Check other Brands.

NOTE. *Always check labels.*—ingredients may change from one week to the next. Do not use margarine in any home-baked cakes, etc. Do not use cake mixes. Do not use Kool-Ade or canned drinks (Hi-C, etc.).

[This is not a complete list of everything allowed on the K-P Diet, but is intended only as a shopping aid, and does not eliminate foods with natural salicylates.]

Good luck.

Mr. HOBART. As a result of our efforts in regard to hyperactive children, we are convinced that Dr. Feingold's hypothesis is absolutely correct.

We have determined, however, that much more work is needed in the area of artificial colors and flavors to determine specifically those chemical additives which are creating the symptoms evident in hyperactive children.

We would hope that the Federal Government, particularly through the Food and Drug Administration, would make adequate appropriations to finance studies in this area.

From a practical standpoint, we are also most concerned that labeling be required to assist parents who have their children on this diet. We believe that there should be some easily identifiable symbol on all products free of artificial colors and flavors. Further, we are concerned that many children who could be greatly helped by the elimination of artificial colors and flavors will not be benefited because of the fact that either their parents are not aware of or are not interested in giving their children the advantages that can be attained by use of the diet.

At the present time, there is little that can be done for these children unless all artificial colors and flavors are removed from our food supply.

We recognize that this remedy is highly improbable and, as an alternative, we are suggesting that labeling requirements of the Food and Drug Administration be amended to include specific ingredients in the products instead of generic terms such as "flavors," "artificial flavors," "color," "spices," and the like.

We have personal experience that our daughter is not affected by vanillin, but it seems to be the case that most children with a sensitivity are affected by this flavor. If this is the case, then there may be other ingredients that parents can find that do not affect their children but do affect other children.

Without specific reference to the artificial ingredients, parents will not have the opportunity to make such a determination.

Incidentally, the same argument can be made for allergy as for the sensitivity we are discussing.

One final point that should be made is that school lunches, many of which are federally financed, seem to play a major role in this area. We know of several instances where children have displayed the symptoms of hyperactivity in particular after they have eaten lunches furnished in the school.

There are several cases of which we are aware that the major problem seemed to have developed after eating at school.

We believe that the Federal Government should examine the food being furnished in the schools to determine whether or not it is affecting the academic performance of the students as well as their discipline.

Thank you, Mr. Chairman.

Senator **KENNEDY**. Thank you very much.

You have made a very complete statement. It is also useful to have your recommendations.

I would like to go on to Mrs. Woodruff.

In your own words, can you tell us how you discovered that your son was hyperkinetic, what some of the steps were which you took, how you heard about this diet, and what the impact has been?

Mr. **WOODRUFF**. We knew right away. We had a feeling that John was very active even when he came home from the hospital. He was kicking every time the car stopped. He would start to kick and cry. It was motion from the word "go" right then and there.

John just had his 16th birthday. We have been searching 16 years for an answer, and especially the last 10 which have been school years.

We have known all along that John is very bright, yet he has worked with a great deal of frustration, especially with homework. The concentration span was not there. It was seeing a bright child and, yet, one who was frustrated with his schoolwork.

We have been on the diet only 2½ months, and are making fantastic progress, I feel. His eyes are sparkling, he is happy, he is relaxed, his coordination has improved so he can now play sports. His attention span is good.

For the first time in John's life, he is doing his homework unaided, without mother sitting there to bring his attention back.

Food program is super easy. It is fun. It is exciting.

The only problems we have are when we travel. We went on vacation this summer, and it was very difficult. A lot of places, well, all they have are Pepsi's. You cannot even get a good old 7-Up, which is permissible.

There were things that, like if you go to a restaurant and you ask about foods and you ask if anything is artificial, they will say no, but they do not know. They think you are bananas, and you do not know what you are talking about.

Something that has concerned us also is that our older boy has just entered college this year, which brought to mind what do we do when all of these children who are bright and will go on to college go to college and live in dormitories and eat in dining halls?

It is a very real problem.

But I think, best of all, John can put it in his own words, how he feels, because he feels so good now.

Senator **KENNEDY**. John, we are glad you are here and we want to thank you for coming this morning to be with us.

We would like for you to tell us a little bit about how you have been feeling since you have been on the diet. We would also like to hear anything else you would like to tell us.

JOHN WOODRUFF. I started the food program in late June this year and found gradual improvement.

First of all, I gradually began to sleep better, which I had not been able to do.

I gradually got rid of unhealthy habits, such as picking new skin around my fingers, and having to wear band-aids due to bleeding.

My sports ability has improved. I have taken up golf and tennis lessons, and now I am beginning to notice improvement and also better coordination in sports and other things.

I have also been told that I am more sociable, more confident and less tense, and most important, that I started school last week and the beginning of my sophomore year in high school, I found it easier to be alert, paid more attention, and was less frustrated than last year during my freshman year.

I believe Dr. Feingold's diet is also helpful to others besides children who are hyperactive. The food program helps people who are more than just hyperactive.

Senator **Kennedy**. Good, John. That is an excellent statement.

Senator **Beall**. How good is your golf?

John Woodruff. I just began. I think I shall improve. I started golf lessons shortly before I went on this food program, and then I began to improve much better than when I had started playing tennis, which was years before I was even on this program.

Senator **Kennedy**. Do you think you are enjoying school a little more this year, John?

John Woodruff. Yes.

Senator **Kennedy**. It is always a tough regimen, I suppose. Do you enjoy your classes somewhat more?

Do you find them somewhat more interesting?

John Woodruff. Yes. It is easier to sit through classes, although sometimes they tend to be boring.

Senator **Kennedy**. Things have not changed much. [Laughter.]

Good, John.

Senator **Beall**. Mrs. Woodruff, had you visited a series of doctors?

Mrs. **Woodruff**. We had gone every place; any place where there was any hope, we went, and never an answer, only frustration from preschool on.

It has been very frustrating. This is the first concrete evidence that we have seen, and so dramatic and so sudden.

Three days after John went on the diet, he came down to breakfast laughing and joking, which was never before.

And, several days after that, then he got a glass of artificially flavored lemonade. Within an hour, there was no doubt, he had become very quiet.

Senator **Beall**. No one in the medical profession which you consulted ever suggested that this may be connected with the diet area?

Mrs. **Woodruff**. No; no one.

Senator **Kennedy**. Mr. Ackerman.

Mr. **Ackerman**. Our human experience in this area, Senator Kennedy, has been a very moving one.

I have two boys. The oldest boy is a delight. He is very well adapted socially and gets along very well in school.

The younger boy struggled with himself for years. One day, late in May several years ago, I was called by the school—they both attend private school in New York City—and was told that there was no hope that the youngest boy could return to school.

No. 1, he was aggressive. He disturbed other children. He was disruptive in play groups. But, specifically, they told me that he would not read, there was no chance he would read. There was a probable chance that he would not write successfully in his lifetime.

I then tried to strike a truce with the school by asking them whether or not they would give him another chance if we sent him to a tutor during the summer and we went to see a psychologist or psychiatrist, whatever was necessary.

The school had recommended both courses.

They then threw the curve ball and said they would accept all of that provided we put your son on drugs.

I asked what was necessary? And they said we would find out from whatever doctor we talked to, and they wanted to be in touch with that doctor.

We then began a merry-go-round of visits to New York City physicians, visited physicians out of town, found that one doctor's diagnosis disagreed with another doctor's diagnosis. But the one thing they all agreed upon was that drugs was the way to solve this problem.

So, for several years, my son was on drugs and became a child continuing to struggle with himself, although he showed improvement in school.

In January of this year, I contacted Dr. Feingold as a result of the piece I saw in one of the national magazines, and spoke with him on the phone. And when he came to New York, we met on Friday evening and liked each other so much, and the next day I asked him if he would come to the house, just to meet my child and tell us what he thought.

He said, "You know, I think he ought to go on my diet. We ought to try it." He said, "If there is any one thing I can see about your son, it is that he is basically an affectionate child."

This was hard for us to see and understand. He was a child that picked on his older brother, caused his older brother some problems in school. His older brother had very good friends, and he constantly remarked that his older brother had more friends; he could not understand why he did not.

We decided to go ahead with the diet. What happened was nearly miraculous.

Within a matter of 6 or 7 weeks, he was reading paragraphs at a clip, he was writing beautifully, he was a happier child and, most importantly, he was showing a lot of affection to the people around him.

I have his report card for last year, which I think is very interesting. Bear in mind this is a child who was told he would not read and probably could not write. They say in here that he is an excellent performer in whatever he wants to do. He is a credit to the school. He has new friends. His work shows progress. I could go on and on.

What we found here, after years of living in darkness with a child who obviously was talented and affectionate, is a way to enjoy our child and have our child enjoy life.

We are very grateful to this doctor.

Senator KENNEDY. Very powerful commentary. You never took the drug regimen?

Mr. ACKERMAN. We did, indeed. Several things happened with the drug regimen.

He became soporific. He fell asleep easily. We then had to adjust the dosage. But we did find, as a result of that, that he lost his appetite. He began to lose weight. The weight loss was rather serious. He was a thin child to begin with.

He began to find, night after night, that he could not sleep, and that at 2 and 3 o'clock in the morning he would come in and sit up and want us to talk with him and read to him or play with him.

Subsequently, of course, he could not get up for school.

This was a great strain, not only on his parents, but other members of the family as well. And the minute we took him off the drug, we saw dramatic changes.

Senator KENNEDY. Did you take him off the drug at the time you went on the diet?

Mr. ACKERMAN. No; not initially.

Dr. Feingold recommended that we take him off drugs immediately. We wanted to play it safe, so we waited a week or two until I found out that one of the drugs he had was artificially colored.

I called the head of research at the drug company that manufactured the drug and asked him for some help.

I prefer not to go into that discussion at this time, but it was a very unsatisfactory discussion.

We then took the child off the drug and, as I say, it has made a world of difference.

I might make one point, if I may. What was very interesting is that during one of his infractions, that is to say, a time when he broke the diet, we were sitting in the den helping him with his homework. And suddenly, his handwriting deteriorated. It looked almost as if a 90-year old man were writing the assignment. We asked him whether or not he had eaten anything in school that he should not have. He said, yes, he had gone out and had a candy bar.

The very next day, his handwriting began to improve, and a week later it was back to what it should be.

Senator KENNEDY. Just that kind of variation could have an impact?

Mr. ACKERMAN. Exactly, that sense to be a reasonably common experience among all of us.

Senator KENNEDY. Mr. and Mrs. Morrison.

Mr. MORRISON. Senators, we are really the second generation here. We have not had the experience these people had.

Our child was caught very young, at 2. I think we have a couple of lessons we can pass on.

Senator KENNEDY. How old is your child?

Mr. MORRISON. Two and a half now. He has been on the diet for 6 months.

I talked to Dr. Feingold by telephone. I want to follow up Mr. Ackerman's statement that we are very grateful to this man.

Our pediatrician recognized that something was wrong. He said, "Hey, let's not try drugs. Let's look for something else." He said, "Try taking him off dairy products for awhile."

We first learned about Dr. Feingold through the New York Times. We brought that up to our pediatrician, and he said "Let's give it a try. What do we have to lose? It just means giving the child nutritious food."

The result was dramatic. The lesson to me is since all Dr. Feingold is saying is give the child fresh fruits and vegetables and healthy food, why not try it before the kid goes on drugs?

The second thing I would like to pass on—my hobby is cooking, and I would like to tell you what my big problem is.

My big problem right now is dairy foods. They do not have to label them. Cheeses are not labeled. Unfortunately, it is mostly high protein stuff. It is a big problem. The other is nebulous labeling—spices.

Mrs. Morrison. Or just flavorings.

Mr. Morrison. Or just flavorings.

But what does that mean? We can cope with that. If it says spices, it goes back on the shelf.

But Travis is getting to the point where he goes to the homes of little friends, and it is a big problem for their parents. They are never sure.

We had one of those unfortunate things, exactly what we heard here, four times today—he came in and was [indicating]—there was obviously a violation.

We went next door and asked our neighbor, and it was something that was improperly labeled. She felt dreadful about it. She was terribly apologetic. What are the people to do?

The label is not clear.

Senator Beall. Do I understand from all the witnesses, other than the Morrisons, that all the children involved at one time were on drugs, drug treatment?

Mr. Hathaway. No, sir. David was never on drugs.

Mrs. Woodruff. John was never on drugs. It was not a discipline problem. He just sat in school and did nothing.

Senator Beall. Those that were on drugs, were they prescribed by physicians?

Mrs. Otis. Yes.

Senator Beall. Do I understand the drugs themselves contained, in some instances, additives that may have been exacerbating the problem rather than helping?

Mr. Ackerman. Exactly.

Senator Kennedy. Raymond, we did not call on you to say anything, but we are awfully glad you are here.

Are you feeling pretty good these days?

You can answer.

Mrs. Otis. It is that butter, Senator. I am dead serious. Every piece of cooking that is publicly offered is contaminated with colored butter, and I would like to use the word "poison."

Raymond feels fine, do you not?

Raymond Otis. Yes.

Mrs. Otis. Raymond wanted a five-speed bike. He started saving up and he had a pretty good bank account. But his father and I could not quite bring ourselves to the risk of allowing him, in his disturbed state, to ride a five-speed bicycle on the street.

He has got one now, though.

Senator Kennedy. You like that bike?

Raymond Otis. Yep.

Senator Kennedy. Well, we want to thank all of you for coming here this morning.

I think it is difficult to talk about some of these past problems. We are very hopeful that, on the basis of the kind of testimony you gave us, we can help a lot of other people.

I think that at the end of this hearing Dr. Feingold's telephone is going to be ringing an awful lot. Many people are becoming aware of the kind of results that you have experienced. From listening to Dr. Feingold and from knowing of his career it seems that he is glad to help whoever he can.

We want to thank particularly our young witnesses, John, David and Raymond, for coming with us. You have been very helpful to us here.

I want to thank all of you very, very much.

Our next witness will be Alexander M. Schmidt, Commissioner, Food and Drug Administration.

We want to welcome you here, Mr. Commissioner. I know you have heard the rather extraordinary kind of testimony that we heard from Dr. Feingold this morning. You are aware of his experiences and studies.

We heard enormously moving and impressive testimony from a number of different people who have come to very similar conclusions based on their experiences with this diet.

We probably cannot say that the research and data in this area is conclusive, but I think that, on the basis of what we have heard this morning, we ought to run this out conclusively to find out whether this diet is something that offers hope to hundred of thousands, maybe millions, of Americans.

I am just wondering what the FDA feels it should do in order to come up with some final conclusions on this study. I am also wondering whether there needs to be additional legislative action and whether additional resources are needed.

I am sure you will find a very positive response here in trying to support whatever is necessary to run this line all the way up.

We are looking to you to see what can be done immediately. And if we need some additional help, what do you feel we can do?

STATEMENT OF ALEXANDER M. SCHMIDT, M.D., COMMISSIONER, FOOD AND DRUG ADMINISTRATION; ACCOMPANIED BY HOWARD R. ROBERTS, PH. D., ACTING DIRECTOR, BUREAU OF FOODS, FDA; AND ALBERT C. KOLBYE, JR., M.D., M.P.A., J.D., ASSOCIATE DIRECTOR FOR SCIENCES, BUREAU OF FOODS, FDA

Dr. SCHMIDT. Thank you, Mr. Chairman.

I do have a brief formal statement that I would prefer just to submit for the record.

Senator KENNEDY. Yes, just submit it for the record. It will be printed in its entirety at the conclusion of your testimony.

Dr. SCHMIDT. I will just make a few brief comments.

I think that the hearing is obviously on a very important subject, and the testimony you have heard this morning is very powerful and moving, as you suggested.

I am sorry that Senator Beall got the impression—probably from a letter that I read and I could see how he might get the impression—

that we, at one point, may have been disinterested in the subject, but I quickly assure you that that has not been the case. I think that the problem was probably professional disinterest, that is, waiting for results from studies before making a commitment.

We are aware of and we share the great interest that Dr. Feingold has generated—that this most difficult subject is now generating. We also share everyone's desire to get the answers to the question that Dr. Feingold has posed.

I would emphasize some of the points that Dr. Feingold made. There are really two areas of exploration that he has identified. One is the study of the etiology of this difficult subject. In studying the etiology of hyperkinesis, one may have to tackle a job as big as studying 1,500 different flavor compounds with very complicated, expensive, and long toxicological tests. So this is obviously a very large and very expensive undertaking, and is clearly beyond what the Food and Drug Administration can do right now.

The second area is that of studying whether or not the diet is effective in treatment. For this we can take the approach of not needing to have all the answers to the questions about hyperkinesis. Perhaps the easiest and most practical thing that can be done in the research area is to proceed with studies examining the thesis in larger numbers of children involving carefully designed and controlled studies.

I think we are all familiar with the need to rule out placebo effects, which are the major difficulty with these kinds of studies.

We agree that the Conners' study is of great interest and needs to be followed by larger studies. It has been estimated that perhaps as many as 80 children should be involved in the next phase of the study so that statistically valid results can be presented to the scientific community.

Senator **KENNEDY**. Let me ask you, does your answer mean that you are going to do a study on the question of the effectiveness of the diet?

Dr. **SCHMIDT**. We have done two things, as Dr. Feingold mentioned. At Assistant Secretary Cooper's direction, I established an interagency committee that is now consulting with the scientists who are doing the studies.

Senator **KENNEDY**. Tell us about that.

Dr. **SCHMIDT**. We have spoken with Dr. Conners, who intends to proceed with his studies, and have discussed with Dr. Feingold the requisites for studies of the type he is interested in in school systems, for example, which obviously could involve a large number of children.

Senator **KENNEDY**. How extensive will those studies be and over what period of time will they be done?

Do you have the money to go ahead?

What are the problems in going ahead?

Is everything on track now?

Dr. **SCHMIDT**. We are consulting with the scientists and encouraging studies to be planned and proposals to be submitted to the Government.

Senator **KENNEDY**. What do you mean by encouraging scientists? Do you have requests in this particular area?

Dr. **SCHMIDT**. The exact status of the Conners' study, perhaps I could ask Dr. Roberts or Dr. Kolbye.

Dr. **ROBERTS**. I think Dr. Kolbye could comment more fully.

Senator **KENNEDY**. What is your name?

Dr. **SCHMIDT**. This is Dr. Kolbye.

Senator KENNEDY. You know what I am driving at, Doctor.

We have heard very impressive testimony here that may very well be a key to a lot of relief of pain, anguish and suffering.

But we obviously do not want to raise false hopes. We want to run this thing out and test it. It seems to me that the work ought to be done on a priority basis.

We want to find out if you are doing the work and we want to assure you that we help you in any way. If you are not doing the work, we want to know why; is it because of lack of funds or authority or what?

We want to get about the business of fulfilling our responsibility.

We also want to hold you, the FDA, accountable for the study, if a study is what is needed. Tell us if the studies are being done, over what period of time they are being done, and when the results will come in?

Dr. KOLBYE. Senator Kennedy, I guess the quick answer to your question is that we are getting ourselves together.

Senator KENNEDY. You have to do better than that.

Dr. KOLBYE. I know. I will come to more specific aspects.

It is a complex problem that ranges in terms of considerations of etiology, diagnosis and treatment. There are various interested agencies within the Federal establishment, including several at the National Institutes of Health, the Food and Drug Administration, the National Institute of Education, the Office of Maternal Child Health, which are all cooperating on this interagency panel.

The tasks that face us are, No. 1, to be aware of all ongoing and proposed research; No. 2, to evaluate these protocols; No. 3, to make our own determinations as to which research should be given priority and how the experimental design should be set up.

Then follows a determination of what magnitude of funding requirements are going to be involved in specific studies, and then follows the question of who has available resources to provide support.

Senator KENNEDY. How long will it take?

How long is this process going to take?

Dr. KOLBYE. We have had one meeting and we are meeting again later this month. I would predict that in a month and a half we will probably be at the stage of making preliminary findings and recommendations about which research directions to become more initimately involved with.

Senator KENNEDY. So that means what?

The one thing I do not think we are going to tolerate is a mishmash of various governmental agencies all attempting to get a piece of the action. Every one of us who has been around here for any period of time, and even those who have not been around here for any period of time, can understand that things fall through the cracks and everybody wants to work from their own point of view.

It is going to be done, I tthink, by the Commissioner of the Food and Drug Administration indicating that this is a priority item, that the FDA is behind this work and that it wants to get some action on it.

Dr. Feingold has his diet. As the Commissioner pointed out, first, you want to find out the effectiveness of this particular kind of diet. And second, you want to study the impact of the other factors that he mentioned.

We can understand that this is a complex issue.

I hope that we get some thoughts from you about the importance of this diet and some recommendation on what really needs to be done. We ought to have a hearing to make a determination of what has to be done.

Dr. Feingold has a diet. It has been effective in a limited number of cases. There are an awful lot of people who are suffering. There is going to be another meeting of the interagency group and there are going to be some protocols issued.

Why can we not do an evaluation on that particular diet?

Why do you not have Dr. Feingold draw up specs on it? He is the one who has done the research; he is the one who is providing relief with the diet. Why is it so complicated?

Why can we not make the expenditure? I mean, if it is $50,000 or $100,000, we can have a flier on something and that may very well make a great difference. We heard yesterday that we are spending an awful lot of money on things that are tested as well as on things that are not being tested. We heard yesterday that we do not have overview and supervision where we are spending hundreds and thousands of dollars in effecting and destroying people's lives.

Here we have something that can really provide relief and we are finding out it is going to be over-supervised.

I do not know if that is a fair characterization, Commissioner. We want to give you a sense of urgency, which I am sure you already have gotten.

Dr. **Schmidt**. I am sure it is not fair.

It is because of my interest that I went to the Secretary and had this interagency group established. The purpose of getting it established would be so that there would be one point that anyone who wished to come to the Government for funding could come to us and not get a run around.

The reason the interagency group was established was so that a protocol that answers the questions posed by the Conners study could be studied by the next study.

It is a very complex thing and great care will have to be taken with the protocol of a large study so that the study is not wasted.

The interagency group will consult with researchers so that the design will be valid. The group will then make recommendations as to the extent of the dollar commitment of the Federal Government toward this effort.

The interagency group will recommend whether or not studies be done by the Government or whether the Government encourage private researchers in universities and so on to come in with proposals, funded by the National Institutes of Health.

The interagency group is a mechanism by which decisions can be made quickly in a single place.

It is a very important step. The Food and Drug Administration, as you know has a very paltry research budget.

Senator **Kennedy**. Well, this is what we want to find out. We applaud the efforts you have made and the leadership you have taken in this. But you and I know that when the Department of Defense wants something done, they go on out and get various Defense contractors in the room, so to speak, and say, "this is what we need in terms of defense system, weapons system or whatever, go on out and get the job done and come on back."

They go say this is what we want, this is the area we want tested.

I am just wondering why it is impossible, prior to the next meeting, to have this interagency group find out who is qualified or not qualified in this general area, they tell these people what we want done and have them go on out to do it. Take the narrow area first.

I do not think there is any question that if you examine all of the points that Dr. Feingold mentioned—all the implications, you know—the work would be very extensive. We ought to find out if such extensive work should be done. But on this narrow area why can we not move ahead and come up with some research that either supports Feingold's conclusion or refutes them.

So then we can do it.

Dr. **Schmidt**. The problem is not in identifying those who are capable of or interested in doing the study. The interagency group's next task is to do, in effect, what you have just said, and that is determine the criteria for the research to be done and evaluate requests for the proposal, for the research.

Senator **Kennedy**. Dr. Feingold, how long do you think it would take to draw up a protocol for a research group?

Dr. **Feingold**. I think the great difficulty is this, as I said in the meeting of the interagency panel no one seems to have any authority to act. It is shifting from one agency to another, saying they do not have jurisdiction to do this or that.

I have recommended that we can zero in on this problem to confirm it, to validate what we are talking about. I can get some of the outstanding scientists in the world actually who are interested and within 6 months, I think, we can definitely demonstrate the validity of the hypothesis and also get some information on colors, which I think are the worst culprits. If we have the authority, if we have the funds——

Senator **Kennedy**. How much money do you think it would cost?

Dr. **Feingold**. Under $100,000. I do not know precisely, but if I had the word to go ahead, I can get that started within a few weeks.

Senator **Kennedy**. This is a loaded question now, Commissioner, but let us take a crack at it. Why can you not do it the way that has been suggested?

Dr. **Schmidt**. I met with Dr. Feingold, and we went over what, in effect, he has just said.

I said, "Fine, I need to react to your proposal. Let me have your proposal." He said, as I recall, that he was not interested in being other than a consultant at this point. And I said, "Fine, we must have a proposal to react to, that is scientifically sound."

We invited that, and we have certainly not done anything but try to stimulate this kind of work including, working with Dr. Conners in his expanded study, which should answer some of the questions raised by the first study.

Senator **Kennedy**. I will let you respond just briefly, Dr Feingold, and then we will continue with Dr. Schmidt.

Dr. **Feingold**. I met the Commissioner June 11. I met with the interagency panel on August 26 or 27. At that time I made my proposal. Dr. Kolbye was in charge.

I said we can do this, I can get two scientists who are outstanding, Dr. Marvin, from the University of California, who is a very well-known human nutritional scientist, and Dr. Bernard Weiss, of the University of Rochester, who will go along with me. Dr. Kolbye said to submit this to us in writing at the next meeting of the interagency panel and we will look at it, talk about it and let me know.

Senator KENNEDY. So that is where it is?

Dr. FEINGOLD. I said let us get it going.

Senator KENNEDY. You are going to submit in writing at the next meeting——

Dr. FEINGOLD. I do not know when the next meeting is.

Senator KENNEDY. What is the date?

Dr. SCHMIDT. Let me be very clear to Dr. Feingold and to you. The Food and Drug Administration is not in the business of making scientific decisions casually. I respect Dr. Feingold, but his casual approach will not answer the scientific question, that is why we have said please submit the scientific protocol.

Senator KENNEDY. Give me the time when the next meeting is.

Dr. SCHMIDT. The next meeting is September 30.

Senator KENNEDY. Dr. Feingold, you are going to have it all written up?

Dr. FEINGOLD. I can have it in the next week or ten days.

Senator KENNEDY. You are going to have to. The time is going on.

Dr. FEINGOLD. I will have it.

Senator KENNEDY. Those interagency meetings are open in any event, are they not?

Dr. SCHMIDT. Yes, sir.

Senator KENNEDY. We will be terribly interested in the results of the meeting. We will try to follow it and work with the Commissioner and with you, Doctor.

Dr. FEINGOLD. I will get on it immediately.

Senator BEALL. Since Dr. Schmidt made an observation about my observation, I think we ought to clear up these observations so we understand each other.

What I was saying was that in 1973 when we first met with Dr. Feingold and got interested in this problem and went to FDA, there was—the reaction of FDA was both skeptical and negative to our request that you investigate Dr. Feingold's hypothesis. As a matter of fact, in the 1975 article in the New York Times, February 9 article in the New York Times, which I submitted for the record, the chief of your own department of color additives says it is true that at first we were "skeptical." It is my understanding that you were no longer skeptical as an agency, but now rather than being skeptical, your scientific curiosity has been aroused and you think the matter is worthy of pursuing.

Dr. SCHMIDT. I think everything you have said is true. I think a hallmark of a scientist is a healthy skepticism, so we remain skeptical about some questions.

Senator BEALL. But not inactive.

Dr. SCHMIDT. We are not disinterested. We are enthusiastic about proceeding ahead.

Senator BEALL. Let me ask a further question. It seems to me I can understand the necessity of proving the hypothesis before we get the public all aroused about these things, but I am disturbed sometimes about the necessity to engage in scientific explanation over an extended period of time. People seem to work with rats and mice, et cetera, when human beings have problems. While they are important, we should not lose the opportunities through the school system, just by picking out one school, and I think Dr. Feingold has testified that in some schools as many as 40 percent of the students may be hyperactive, and in that case it would seem to be very simple, under the proper guidance, for scientifically oriented people to go into a school and select some students and run the test and see if the hypothesis holds up, would that not be a worthy endeavor?

Dr. SCHMIDT. That kind of study can be done. It is my personal view that that type of study should be done and it will be done.

Senator BEALL. And can be done very expeditiously at probably minimal costs, can it not?

Dr. SCHMIDT. I could not venture a guess about the cost. I really do not know what it would cost in terms of dietary control and very precise observations that would have to be made, but it would not be exorbitant.

Senator BEALL. It would not take very long?

Dr. SCHMIDT. It would not be prohibitive.

Senator BEALL. It would not take very long I say?

Dr. SCHMIDT. I would not think so.

Senator BEALL. Has any study ever been made as to the effectiveness of drugs in the treatment of hyperactivity?

Dr. SCHMIDT. Yes.

Senator BEALL. Do you know what the success rate is?

Dr. SCHMIDT. We have been very concerned about the use of drugs. As a matter of fact, some of our panels have done some very important work in precise definitions of the clinical syndromes and measurement tools to judge the efficacy of drugs.

The success rate I think is as hard to pinpoint with drugs as it is with any other kind of intervention. It varies little with the different kinds of stimulants. I understand the success rate of drugs is about 75 percent——

Senator BEALL. Seventy-five percent of what?

Dr. SCHMIDT. Seventy-five percent of children would have some beneficial effect.

Senator BEALL. Have been helped by drugs?

Dr. SCHMIDT. Yes.

Senator BEALL. It would be easy, therefore, since some tests have been conducted with drugs to compare the effects of drugs as opposed to Dr. Feingold's hypothesis, put them side by side, could you not?

Dr. SCHMIDT. If one wished to study comparative efficacy of drugs versus——

Senator BEALL. That is a valid comparison, is it not?

Dr. SCHMIDT. That would have to be a very complex study. Because in every study like this, control groups would have to be included, but that kind of triple crossover study could be done. It is not necessary to examine the validity of the diet treatment.

Senator KENNEDY. Commissioner, under section 409 of the Food and Drug Cosmetic Act, it gives authority concerning food additives, and the presumption is that food additives would be deemed unsafe unless the additive is in conformity with FDA regulations for safe use.

What is the nature of those regulations? How do we know these things are safe?

Dr. Feingold thinks there are very significant questions to be raised. He points out that we do not know what the long term metabolic impact from these additives is on any child or grownup.

Dr. SCHMIDT. My answer is precisely the same answer as Dr. Feingold's. He pointed out that food additives, artificial flavors and colors, many of which are identical to the natural compound, have been around for many years.

Dr. Feingold said, or implied, that we are at a new point in history as far as our society definition of safety goes, and certainly insofar as our ability to determine things scientifically is concerned.

Dr. Feingold suggested——

Senator KENNEDY. Leave Dr. Feingold out.

Dr. SCHMIDT. Well, as you know, we are engaged in a review of all the knowledge accumulated to date on the safety of food additives.

Depending on what we discover by this review, different things will be done with regard to food additives. We are clearly being stricter now in accepting evidence submitted to us in food additive petitions to prove safety.

The kind of studies being done now include metabolic studies, and I think, probably most kinds of things that could be done to prove safety.

What is also a fact is that there are many things that have not been subjected to the kind of studies that we now require before we approve a food petition. Thus, there is an immense job of doubling back and working through on some kind of priority basis, the list of thousands of chemicals that are in use. If we are to do this, since you asked about need, it is clear that we would need a lot of people and a lot of money to do this.

Senator KENNEDY. Do you not think we ought to know how many people and how much money is needed and what the health implications are?

I will give all the help I possibly can in assuring that that is the case. I think you can get support for that.

Dr. SCHMIDT. There is another area, since you asked about things——

Senator KENNEDY. How long is it going to take at the present time with the manpower and the budget that you have at the present time?

Dr. SCHMIDT. Well, as of now, we cannot do the job.

Senator KENNEDY. What does that mean in terms of the health of the American people? That is a very serious admission, very serious admission. I do not question your own sincerity.

Dr. SCHMIDT. You are raising the question of what is the purpose of the Food and Drug Administration?

Senator KENNEDY. I am raising it specifically with regard to the issue of these food additives and potential dangers.

Dr. SCHMIDT. Let us be specific. There are probably 1,500 different flavor substances. Dr. Feingold said that probably none had been studied extensively for toxicological effects.

For purposes of discussion, I will agree that there may be safety questions to be answered. Now, the question is, Who says what studies ought to be done? My answer is that the Food and Drug Administration should.

The next question is, Who should do those studies?

And the third question is, Who should pay for them?

As for doing them, we do not have facilities, the manpower, the money, or the mandate to do those studies. As we have said many times in hearings, we have always imposed requirements on industry. The Congress has put the burden of proof of safety on the industry.

So we are saying, then, in effect, that we should require all of these studies to be done by or paid for by industry, and this will impact on the price of the goods.

Now, these are the kinds of questions that have to be thought through in order to answer your question.

General statements and sweeping statements are easy to make, but one has to go into great detail and think through the steps before he can respond in a reasonable way.

I think at some distant date we will know everything we ought to know about every environmental chemical. But we have a history in this country—that regulatory agencies are probably responsible for in part, but only in part—and we have to work through the problems that have accumulated throughout our history and are left with us now.

One other area is that of labeling. People can go on the diet now, as has been pointed out, but they need to know what is in the food. We have mandatory ingredient labeling for foods and as I have said many times, I am in favor of full and informative labeling.

What I have found in many instances is that the Congress, for reasons that I do not know, has written in exemptions which prevent us from solving the cheese problem, the ice cream problem and——

Senator KENNEDY. I can tell you what the reason is: it is the power of special interests, the large campaign contributions to Members of Congress and the Senate.

Dr. SCHMIDT. I have asked some oldtimers, and they have said, "Well, ice cream, cheese, and butter—there are answers, but these exemptions right now prohibit us." I feel rather silly sometimes answering my mail, because I get letters that are as poignant as the testimony we have heard today.

I have to write back and say I am sorry, there is no way that what you want can happen, because it is against the law. It is against the law for there to be a declaration for some ingredients on some labeling.

We have asked for changes in that law, and this is an area that we would hope to explore with you in order to remove some of these exemptions.

If food were labeled so that parents could tell, then the biggest single impediment to the use of the diet would be removed. Meanwhile, we could be doing the school studies and the other studies.

Senator BEALL. On that point, you have the authority now to put a logo on a box that would indicate there are no food additives?

Dr. SCHMIDT. No, sir.

My wife buys strawberry jam, and it says on the label that it contains nothing but strawberries. I request her to buy that. That is legal.

A logo that signifies there are no artificial flavors or colors on a label would be legal, and we have said so publicly, and told Dr. Feingold and others that this may be done. We do not require it.

The logo can be used. We cannot require it, nor could we permit the logo to be used to promote a product.

Senator Beall. Would you support legislation that mandated it?

Dr. Schmidt. I would prefer to support legislation that mandated affirmative disclosure of what is in these things, and that would render a logo, which is kind of a dumb thing, really, useless or needless.

The reason the logo is important is that it is the next best thing to do.

Senator Beall. I do not want to get into an argument of what is better. Maybe it would be better to have all the items itemized on the carton, but at the same time it seems to me these people are interested in knowing if something has nothing in it.

Would it not make sense to have a logo to say—well, excuse me for saying "nothing," nothing artificial—no artificial additives, or colors.

Would it not make sense to, if you had a logo, instead of reading through the list——

Dr. Schmidt. No; I do not think the logo is the better choice. The reason for that is, you heard one of the parents say that for his child this was all right, and this was not, and for another child, that is different.

What has not been brought up this morning is that besides artificial flavors and artificial colors, salicylates, other food radicals, other substances in the food, and trace metals have been implicated also.

Now, you see the problem becomes then, What does a logo define?

Some parents would not be helped by a logo, I would guess. What they would be helped by is knowing precisely what is in that bottle, and that is why I would favor full and informative disclosure.

I think Dr. Feingold would agree with me that——

Dr. Feingold. I do not agree.

Dr. Schmidt [continuing]. That a logo is not as satisfactory as full disclosure.

He does not agree.

Dr. Feingold. I am sorry, Commissioner. I have to take issue with you. We are talking about two different problems.

You are inferring that any compound can induce an adverse reaction, whether it is natural or synthetic, it makes no difference.

It is true there are other compounds. We are addressing ourselves to one simple issue here, colors and flavors, which we feel represent the cause of perhaps 40 or 50 percent of these children.

Even if you have full disclosure, I am sure you have tried, your wife has tried, to go to the marketplace and read those labels, and it is not legible. It is on the crinkling edge of the paper, and I say if we put a logo on, it is going to help this problem, and the issues are not the same at all.

It is not stupid. I think it is very bright.

Dr. Schmidt. Certainly the logo is permissible.

Senator Kennedy. Could you not have both.

[Applause.]

Senator Kennedy. That is an old political answer. Have it both ways.

[Laughter.]

Dr. Schmidt. I would just like to say that I am sitting here very uncomfortable, and I think I have two problems.

One is that I have a very unfortunate habit of remembering from hearing to hearing what was said at one hearing, and that at some of your hearing, the point is that the Food and Drug Administration must be the most meticulous observer, the most careful examiner of raw data, the most astute questioner, the most skeptical of all scientists.

OK?

And then I always feel like a "heavy." And I think that sometimes that is justified. And where we are the "heavies" in this, you know we should be prodded and so on. And I think on this one we have taken the initiative to try to organize, even the Public Health Service, which is not easy, and to be responsive, to invite proposals, to seek out researchers, to establish protocol, which is not a usual activity.

I can speak for Dr. Cooper and say that he is, as you are, eager to see these things resolved. I do not think $100,000 is a small amount of money, and I will not see it wasted, but that amount of money is not the problem.

I think that we can, in a relatively short time, satisfy Dr. Feingold's urgent request, and the parents' urgent pleas.

Senator KENNEDY. That is what we are interested in.

Dr. SCHMIDT. I assure you that the Food and Drug Administration is interested in this.

Senator KENNEDY. I think that is an excellent note on which to wind up the hearing.

I just want to mention one thing that is not directly a part of this hearing, but which you touched on, and I think very accurately, Mr. Commissioner.

That is, we are asking the FDA to assume increasing responsibilities. The medical device legislation was passed. The whole area of food and food additives is going to become a major area of public interest.

I am hopeful that you are going to let people like myself and other members of the committee know who is after the Food and Drug Administration in different areas. I am hopeful that you are going to help us to equip you with the resources and the talent to do the job.

We need to have a good understanding. We have to educate the Congress, as well as ourselves perhaps, to the need here.

I think we are really going to need your help in order that we not set unfair criteria which, because of congressional action or lack of action, you do not have the ability to meet.

Finally, I will mention that we did not have representatives from some of the industry people who have been interested in this particular issue. We point out that this is not really a legislative hearing today, even though much of the material that we have gotten here will form the basis for legislation. We want to indicate to the industry people, who obviously have some interest in this, that prior to consideration of legislation they will have an opportunity to have their voices heard.

Senator BEALL. And Dr. Connors.

Senator KENNEDY. Yes, and Dr. Connors.

At this point I ordered printed in the record the prepared statement of Dr. Schmidt and all other statements and material subsequently supplied.

[The material referred to follows:]

STATEMENT

BY

ALEXANDER M. SCHMIDT, M.D.
COMMISSIONER
FOOD AND DRUG ADMINISTRATION
PUBLIC HEALTH SERVICE
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

BEFORE THE
SUBCOMMITTEE ON HEALTH
COMMITTEE ON LABOR AND PUBLIC WELFARE

UNITED STATES SENATE

SEPTEMBER 11, 1975

Mr. Chairman and Members of the Subcommittee:

We are here today to discuss the Food and Drug Administration's (FDA) activities relating to the general problem of hyperkinetic behavior in children and the specific hypothesis that artificial food flavors and colors may cause the condition.

The FDA is aware of the great public interest which has been generated by the hypothesis advanced by Dr. Ben F. Feingold of the Kaiser-Permanente Medical Center in San Francisco. Dr. Feingold contends that a significant percentage of children with hyperkinesis display a dramatic improvement when they are placed on a diet that excludes all food items containing artificial colors and food additives, and certain fruits and vegetables.

We share both the interest that Dr. Feingold's thesis has aroused, and the desire to put Dr. Feingold's thesis to more definitive testing. We have met with Dr. Feingold, and have taken some subsequent action which we believe can lead to a better understanding of this complex and difficult field.

One needs first to beware of some of the problems involved in assessing the hypothesis that has been advanced by Dr. Feingold -- problems which must be overcome when testing in a scientifically credible and convincing manner, any hypothesis -- and several have been advanced -- concerning the hyperkinetic behavior syndrome.

HYPERKINETIC BEHAVIOR SYNDROME

The "hyperkinetic behavior syndrome" refers to a complex group of problems, occurring primarily in children, which are manifested in a manner extremely distressing to families and teachers and to the children themselves. It is a condition that medical science has thus far had difficulty in defining with precision.

Dr. P.H. Wender,[1] of the University of Utah, College of Medicine, notes that there is evidence that several different causes may be involved and that the hyperkinetic behavior syndrome includes a variety of symptoms. Symptoms include:

-- hyperactivity and excitability,

-- short attention span,

-- poor powers of concentration,

-- low tolerance for frustration,

-- diminished ability to experience pleasure, and

-- resistance to disciplinary measures.

Additional difficulties may include impaired ability to learn in areas such as reading, spelling, and visual and motor activities.

FDA has approved various drugs used in therapies which have resulted in symptomatic improvement in children with hyperkinetic behavior. Children with such behavior symptoms often respond well to drugs of the amphetamine class which usually would be stimulating to adults.

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[1] P.H.Wender, M.D., "Some Speculations Concerning a Possible Biochemical Basis of Minimal Brain Dysfunction," Ann. N.Y. Acad. Sci. 205:18, 1973.

Careful use of these drugs is, of course, mandatory; and they treat only symptoms and do not address the causative factors giving rise to these symptoms. The syndrome may eventually prove to have many causes. For example, psychosocial and environmental factors have been implicated, as have diet and nutritional status. Metabolic variations may increase susceptibility to biochemical influences on the central nervous system. Disorders of pregnancy and birth, and subclinical lead encephalopathy have also been suggested as possible factors.

I have pointed out some of these definitional difficulties to illustrate the care with which one must approach the evaluation of clinical research in this field including possibly treatment programs.

The evaluation of results of different treatments have proved as difficult to standardize as the syndrome definition. For example, clinical drug experience indicates that many factors may alter the activity of hyperkinetic children making it difficult for untrained observers to perceive these behavioral changes in the same way as trained observers. Both trained and untrained observers encountered significant placebo effect associated with these clinical trials. All studies involving hyperkinesis must identify any placebo effects. Finally, there are important ethical considerations that must be taken into account in the design of any such experimentation.

While these difficulties are formidible, clinicians and researchers are designing and conducting studies to define better the syndrome and determine its causes and treatment. I believe that if these efforts are vigorously pursued they will lead to rapid advances in treating afflicted children.

A dietary study by Dr. Keith Connors of the University of Pittsburgh has recently been completed. This study was funded by the National Institute of Education (NIE) and the preliminary report is being evaluated.

Dr. Connors studied 15 hyperactive children on a control diet, and an experimental diet eliminating artificial flavors, colors and natural salicylates. The children were randomly [illegible] to one of the diets, and rated in terms of their behavior for a period of four weeks [illegible] their parents and teachers. Then the diet was changed for the next four weeks with the ratings continuing. From the preliminary report, it appears that the teachers noted some reduction of sumptoms on the experimental diet in the group of children first placed on the control diet, but the parents noted less improvement. The design of this study and the data are being evaluated by interested scientists in an interagency collaborative group which Assistant Secretary Cooper asked that I form. Dr. Connors himself has stated, "It would be hazardous at this point to draw too many conclusions from this experiment, given the small size of the sample and the lack of complete consistency in the results. Any thoughtful observer will understand that a major intervention into dietary habits of a family will produce behavioral effects, regardless of the specific diets, a phenomenon well understood in the management of such conditions as juvenile diabetes. The results would have been substantially clarified if it had been possible to have objective measures of function uncontaminated by the psychological factors which are bound to operate in the family-school-child system. At this point, the results point to the need for considerable further investigation."

Another study by J.P. Harley, Ph.D., et al., is underway at the Food Research Institute at the University of Wisconsin in Madison. Thirty male hyperkinetic children, aged 6 to 12, are being studied using control and experimental diets on a crossover basis. Naturally occurring and added salicylates, synthetic food dyes, and artificial flavorings are being eliminated in the experimental diet. During the study the children are being assessed by psychological tests and a rating system based on that also used by Dr. Connors. These approaches to rating are essentially the same as those used in the evaluation of drug therapy for this condition. This study is currently underway and the results are expected to be available early in 1976.

As I have mentioned, we recently formed a new interagency group to review hyperkinesis research and coordinate government effects in this area. This working group has the task of reviewing and assessing completed and ongoing research projects, identifying and exploring research needs, and identifying the particular role of each agency in carrying out or funding such research. The group which includes representatives from the Bureau of Foods and Bureau of Drugs of FDA; National Institute for Mental Health; Office of Education; and the National Institute for Child Health and Human Development, will hold its second meeting this month.

While the definitive answers regarding the causes and treatment of the syndrome are being sought, the FDA is continuing its efforts to increase the information available to consumers regarding food ingredients. For example, we are allowing the use of a label-symbol to advise consumers that products do not contain artificial flavors or colors. This "logo" is voluntarily used by manufacturers -- we have not required its use, nor could we, under our law. We have also encouraged manufacturers to identify voluntarily artificial colors used in nonstandardized foods. Again, however, the present law does not permit us to insist upon such disclosure.

As you know, section 403 of the Food, Drug, and Cosmetic Act does not require label disclosure of all ingredients in all food. The courts have construed section 403(g) as precluding FDA from requiring label designation of mandatory ingredients in standardized foods. Moreover, section 403(e) specifically permits flavorings, preservatives, and coloring ingredients to be designated generically, "without naming each" ingredient. Thus, our authority to act affirmatively to require full ingredient disclosure is somewhat limited.

In summary, we can all appreciate the need for continued attention to this very serious health problem. We believe in the need for a careful consideration of the issues involved, additional well-designed research, and coordinated government effort to support all promising areas of investigation.

Mr. Chairman and Members of the Subcommittee, this concludes my statement. My colleagues and I will be pleased to answer any questions you may have.

ALBERT C. KOLBYE, JR., M.D., M.P.H., J.D.

Associate Director for Sciences
Bureau of Foods
Food and Drug Administration

Provides overall administrative and scientific direction for the Office of Sciences, Bureau of Foods, FDA. Responsible for coordinating the scientific, medical and epidemiological review of all potential health hazards involved in food, including intentional additives as well as environmental contaminants; provides technical oversight for cosmetic and aerosol toxicity.

Born in Philadelphia February 15, 1935. Received A.B. degree from Harvard College in 1957; M.D. from Temple University School of Medicine, Philadelphia in 1961; M.P.H. in chronic disease epidemiology from Johns Hopkins University in 1965 and J.D. in 1966 from the University of Maryland. In 1962 joined the Public Health Service as a member of the Regular Commissioned Corps with the Heart Disease Control Program. Served in that program until 1967 as Acting County Health Officer (Prince George), Medical Consultant and Chief of the Field Staff, Heart Disease Control Program, Bureau of State Services, U. S. Public Health Service. In 1967 appointed Staff Director in the National Clearinghouse for Smoking and Health, and was staff director and/or senior editor for three annual reports to Congress (1967-69), and Special Assistant to the Assistant Secretary for Health and Scientific Affairs, DHEW. In 1969 appointed Director, Office of Standards and Compliance, Consumer Protection and Environmental Health Service and, concurrently, as Staff Director and Executive Secretary for the Secretary's Commission on Pesticides and Their Relationship to Environmental Health. In 1970 appointed as Deputy Director of the then Bureau of Foods, Pesticides and Product Safety. Promotion to rank of Assistant Surgeon General in 1971. Assumed current position as Associate Bureau Director for Sciences, Bureau of Foods, in 1972. Also serves as medical-legal consultant to the Armed Forces Institute of Pathology and the Department of Defense as well as legal counsel to the American Academy of Clinical Toxicology. Has memberships in various scientific and legal associations and is a Fellow of the American College of Legal Medicine, American College of Preventive Medicine, and the American Public Health Association.

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Born:
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Education:
H.S. 1953 - - William Penn Charter School
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A.B. 1957 - - Harvard College
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M.D. 1961 - - Temple University School of Medicine
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Intern 1961-1962 - - University Hospitals
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Resident 1962-1964 - - Preventive Medicine and Public Health
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M.P.H. 1965 - - Chronic Disease Epidemiology, Johns Hopkins University, Baltimore, Maryland
J.D. 1966 - - University of Maryland Law School
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Fellow of:
American Public Health Association (A.P.H.A.)
American College of Legal Medicine (A.C.L.M.)
American College of Preventive Medicine (A.C.P.M.)

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American Academy Forensic Sciences
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Maryland State Bar Association
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Maryland Medical Chirugical Society
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POSITION: Acting Director, Bureau of Foods
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BIRTH DATA: Born July 6, 1932
Eldred, Pennsylvania

EDUCATION: Jamestown Community College, Jamestown, N.Y., 1950 - 1951
The George Washington University, Washington, D.C., 1951 - 1955, B.S. (Math)
The George Washington University, Washington, D.C., 1955 - 1957, M.S. (Math - Statistics)
The George Washington University, Washington, D.C. 1957 - 1962, Ph.D. (Math - Statistics)

EXPERIENCE: FDA

November 1974 - Present
Acting Director, Bureau of Foods

March 1974 - November 1974
Associate Director for Management, Bureau of Foods

February 1972 - March 1974
Director, Division of Mathematics, Bureau of Foods

January 1972
Consultant (Mathematical Statistician), Bureau of Foods

Booz, Allen & Hamilton, Inc.

1970 - 1971
Vice President; Managing Officer, Central Region; BASYS, Inc. - Computer Systems subsidiary of BA & H

1969 - 1970
Vice President; Managing Officer, Kansas City Office; Booz, Allen Applied Research, Inc., - Scientific and Technical Services subsidiary of BA & H

1967 - 1969
Vice President; Washington, D.C. Office; Booz, Allen Applied Research, Inc.

1964 - 1967
Research Director; Washington, D.C. Office; Booz, Allen Applied Research, Inc.

1959 - 1964
Project Scientist; Washington, D.C. Office; Booz, Allen Applied Research, Inc.

The Johns Hopkins University

1958 - 1959
Operations Analyst; Operations Research Office; Bethesda, Maryland

The George Washington University

1958 - 1959
Associate in Statistics; Department of Statistics Faculty

1957 - 1958
University Teaching Fellow; Department of Statistics Faculty

1955 - 1957
Graduate Teaching Assistant; Department of Statistics Faculty

Private Consultant

1955 - 1959
Statistical Consultant to National Canner's Association, Corn Industries Research Foundation, G.W.U. Department of Pharmacology and various trade associations

PROFESSIONAL SOCIETIES

Member Board of Governors, Food Update, Food and Drug Law Institute
American Society for Quality Control -- past chairman, Washington, D.C. Section; past chairman, Electronics Division; senior member
American Statistical Association

HONORS AND AWARDS

Sigma Xi - full member
American Men of Science
Who's Who in the Midwest
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George W. Koch
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David E. Guerrant, President
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The Procter & Gamble Company
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O. Cedric Rowntree, Chairman
The R. T. French Company
Robert M. Schaeberle, Chairman
Nabisco, Inc.
Boyd F. Schenk, Chairman/President
Pet Incorporated
Richard B. Sellars, Chairman
Johnson & Johnson
Harold A. Shaub, President
Campbell Soup Company
Robert B. Shetterly, President
The Clorox Company
Lloyd E. Skinner, Chairman
Skinner Macaroni Company
Paul H. Smucker, Chairman/President
The J. M. Smucker Company
William H. Spoor, Chairman
The Pillsbury Company
J. Paul Sticht, President
R. J. Reynolds Industries, Inc.
Dwight L. Stuart, President
Carnation Company
Robert D. Stuart, Jr., President
The Quaker Oats Company
John C. Suerth, Chairman
Gerber Products Company
Henry Weigl, Chairman
Standard Brands Inc.
Ben H. Wells, Chairman
The Seven-Up Company
Harry K. Wells, President
McCormick & Co., Inc.

October 30, 1975

The Honorable
Edward M. Kennedy
Chairman
Subcommittee on Health
4228 Dirksen Senate
  Office Building
U. S. Senate
Washington, D.C. 20510

Dear Mr. Chairman:

We are pleased to submit the enclosed statement for the record of the "Joint Subcommittee Hearings On A New Method Of Treating Hyperactive Children."

GMA appreciates the opportunity to provide comments for the hearing record.

Sincerely,

George W. Koch

George W. Koch

GWK/fb

Enclosure

Grocery Manufacturers of America, Inc., 1425 K St., N.W., Washington, D. C. 20005 · (202) 638-6100

STATEMENT
# of the
GROCERY MANUFACTURERS OF AMERICA, INC.
to the
SUBCOMMITTEE ON HEALTH
# of the
SENATE COMMITTEE ON LABOR AND PUBLIC WELFARE

October 30, 1975

More than anything else, the Grocery Manufacturers of America wishes to show its deep felt concern over, and share its knowledge of, the critically important subject of the relation of the diet to hyperactivity in children. We regret that we, as well as others who have approached this subject from a scientific standpoint, have been denied an adequate opportunity to do so.

We are not sure who will benefit from the recent Joint Subcommittee hearings on this subject, but we cannot help but be saddened by the feeling that the children and their concerned parents who are in most need of help were not.

GMA is the trade association for the leading manufacturers of grocery products. We appreciate this opportunity extended by Senator Javits to submit a statement for the record after the hearings.

We advocate only one point of view -- the essentiality of a determined scientific effort to find and eliminate the cause of hyperkinesis.

Such an inquiry should, as its first order of priority, study the hyperkinesis-diet hypothesis advanced by Dr. Ben F. Feingold. Perhaps now, after the publicity generated by the Joint Subcommittee hearings, it should also address itself to a question left unasked during your forum: "What if Dr. Feingold's theory is not correct?"

There have been at least three groups convened by various parties to examine the hyperkinesis-diet hypothesis. The reports of two of these groups, the GMA expert panel and the National Advisory Committee on Hyperkinesis and Food Additives, are available. The report of the third group, the Interagency Group on Hyperkinesis of the Department of Health, Education and Welfare, is expected in the next few weeks.

The first group to examine the reports of Ben F. Feingold, M.D., was brought together by GMA in the fall of 1973. The group's report of March 28, 1974, includes the following summary:

> We have examined the manuscript entitled "Adverse Reactions to Food Additives With Special Reference to Hyperkinesis and Learning Difficulty (H-LD)" as prepared by Dr. Ben F. Feingold and published in the Congressional Record of October 30, 1973 (S.19736-19742). Because of a number of serious deficiencies in the experimental design and/or in the reporting of clinical observations in this manuscript, plus the availability of information and reasoning pointing in other directions, we find almost wholly without support the hypothesis put forward by Dr. Feingold that food additives are linked to H-LD. At the same time, one cannot state categorically that there is no relationship between ingestion of food additives and hyperkinesis and learning disorders.
>
> The Feingold manuscript asserts that there is a relationship; this relationship has not been scientifically demonstrated. The design of a rigorous study to evaluate this concept is compatible with the continuing need to assure that every precaution is taken to protect the public health.

The full report, entitled "Critique of Manuscript by Ben F. Feingold, M.D., Entitled 'Adverse Reactions to Food Additives'", is enclosed for the record.

The second group, the National Advisory Committee on Hyperkinesis and Food Additives, was brought together under the auspices of The Nutrition Foundation in January of this year. The Advisory Committee consisted of fourteen highly respected scientists from academic and professional organizations. The Committee was charged with three responsibilities:

(a) review critically and objectively the nature of evidence relative to the hypothesized relationship; (b) recommend whether additional investigations were justified or desirable; and if so, (c) provide guidelines for the experimental design of appropriate studies which would result in obtaining valid data upon which conclusions might be formulated.

The summary of the Committee's deliberations is succinct:

> The Committee concludes that data from critically designed and executed studies, free of the deficiencies of design noted, must be available before firm conclusions can be reached on the Feingold hypothesis. Accordingly, the Committee has considered at length the experimental design characteristics necessary to obtain definitive, interpretable data which may permit a decisive interpretation.

A copy of the Report to The Nutrition Foundation by the National Advisory Committee on Hyperkinesis and Food Additives is enclosed for the record.

The Interagency Group on Hyperkinesis is expected to prepare a report for submission to Dr. Theodore Cooper, Assistant Secretary for Health, HEW, by October 31, 1975. Based on the Transcript of Proceedings of the Group's meeting of September 30, 1975, it appears that the Interagency Group will recommend that additional research be conducted. This would be a recommendation parallel to and consistent with the reports prepared by the GMA expert panel and the National Advisory Committee.

Dr. Alexander M. Schmidt, Commissioner of the Food and Drug Administration, noted in his testimony before the Subcommittee that the hyperkinetic behavior syndrome is a condition that medical science has thus far had difficulty in defining with precision. He further told the Subcommittee:

> The evaluation of results of different treatments have (sic) proved as difficult to standardize as the syndrome definition. For example, clinical drug experience indicates that many factors may alter the activity of hyperkinetic children making it difficult for untrained observers to perceive these behavioral changes in the same way as trained observers. Both trained and untrained observers encountered significant placebo effect associated with these clinical trials. All studies involving hyperkinesis must identify any placebo effects.

To our knowledge, only one double blind crossover study has been completed in investigating the relationship between hyperkinesis and diet. This study was conducted by Dr. C. Keith Conners of the University of Pittsburgh; both Dr. Feingold and Dr. Schmidt commented on this work during the hearing. Because of the widespread publicity given Dr. Feingold and his work, most the parents of hyperkinetic children involved in the study were aware of Dr. Feingold's dietary hypothesis and recognized the Feingold diet. In the controlled study, five of fifteen children responded to dietary manipulation, but as Dr. Conners has stated (as quoted by Dr. Schmidt):

> It would be hazardous at this point to draw too many conclusions from this experiment, given the small size of the sample and the lack of complete consistency in the results. Any thoughtful observer will understand that a major intervention into dietary habits of a family will produce behavioral effects, regardless of the specific diets, a phenomenon well understood in the management of such conditions as juvenile diabetes.

Thus, there has been only one controlled study completed, and the principal investigator has reservations about drawing conclusions from the study.

Today, there is insufficient evidence to determine whether there is any relationship between hyperkinesis and dietary composition. Whether there is or not, as food manufacturers we are as determined as hyperkinetic children and their parents are to find the cause of hyperkinesis. The food industry is prepared to work independently or in cooperation with the Department of Health, Education and Welfare to investigate and understand the purported relationship between diet and hyperkinesis.

THE NATIONAL ADVISORY COMMITTEE
ON
HYPERKINESIS AND FOOD ADDITIVES

REPORT TO
THE NUTRITION FOUNDATION

June 1, 1975

The National Advisory Committee on Hyperkinesis and Food Additives

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Introduction

Aware of the anxiety created by the publicized hypothesis advanced by Dr. Ben F. Feingold (1) in 1973 implicating many widely distributed or highly nutritious food-stuffs and undesignated food additives as potential factors in hyperkinesis, The Nutrition Foundation has supported a responsible, critical review by a competent group of expert medical and behavioral scientists of evidence relative to this hypothesis. The scientists who comprised the review committee were selected and identified by the offices of major scientific and medical organizations: American Medical Association's Council on Foods and Nutrition; American Psychiatric Association; American Association of Child Psychiatry; Society of Toxicology; Council for Exceptional Children; American Alliance for Health, Physical Education; Institute of Food Technologists; American Society for Clinical Nutrition; American Dietetic Association; The National Nutrition Consortium; Life Sciences Research Office of the Federation of American Societies for Experimental Biology; Committee on Nutrition of the American Academy of Pediatrics; and the Food and Nutrition Board of the National Academy of Sciences.

An intensive literature search seeking all relevant published information was conducted and copies of the published materials were provided each member of the Committee. The published materials were supplemented with manuscripts of talks, research proposals, or other pertinent unpublished information obtainable from any of the participating sources. Immediately prior to the initial meeting of the Committee, the book by Dr. Ben F. Feingold entitled *Why Your Child Is Hyperactive* was published (2) and copies were made available to the conferees attending the first Committee meeting.

The Committee was charged with the responsibility to (a) review critically and objectively the nature of evidence relative to the hypothesized relationship, (b) recommend whether additional investigations were justified or desirable, and, if so, (c) provide guidelines for the experimental design of appropriate studies which would result in obtaining valid data upon which conclusions might be formulated. The background of the committee is such as to provide valuable guidance in assessing evidence and design of any subsequently projected clinical and experimental investigations of the postulated relationship between hyperkinesis and food.

Dr. Morris Lipton, Professor of Psychiatry, University of North Carolina and a member of the American Psychiatric Association was elected Chairman.

An initial meeting was held January 12-14, 1975, at Harrison House in Glen Cove, Long Island. Observer representatives were invited from the Food and Drug Administration, the Ford Foundation, Grocery Manufacturers of America, Inc., National Institute of Education, the National Institutes of Health and from three major food companies. The identity of these observers and their affiliations are listed in the Appendix. The observer from the National Institutes of Health was unable to attend this initial meeting, but has been provided with information exchanged prior and subsequent to the meeting.

Resource personnel were invited who could provide background information, who were knowledgeable concerning or involved in current investigations or were planning research in the area. These included:

Dr. GERALD A. GLEICH, Allergist
The Mayo Clinic
Rochester, Minnesota

Dr. DONALD K. ROUTH, Research Psychologist
Child Development Research Center
University of North Carolina
Chapel Hill, North Carolina

Dr. BEN F. FEINGOLD, Retired Staff Member
Kaiser-Permanente Medical Center
San Francisco, California

and medical and behavioral scientists involved in research and planning of studies at the following centers:

University of Wisconsin:

DR. PETER EICHMAN
Professor of Neurology
Neurological Institute
Madison, Wisconsin

DR. PRESTON HARLEY
Department of Neurology
University of Wisconsin Medical Center
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University of Pittsburgh:

Dr. Charles Goyette
Project Coordinator
Western Psychiatric Institute and Clinic
Pittsburgh, Pennsylvania

Harvard University:

Dr. George Kerr
Associate Professor
Department of Nutrition
Harvard School of Public Health
Boston, Massachusetts

University of Minnesota:

Dr. Michael Appleman
Department of Education
St. Paul, Minnesota

Resource personnel, as well as members of the Advisory Committee, presented relevant background reviews which were followed by free discussion and exchange participated in by all persons in attendance at the meeting. The background discussions pertained to the broad areas of the nature of hyperkinesis; methods of assessing its severity and the effectiveness of therapy; an extended discussion by Dr. Feingold concerning his hypothesis and management regimen; a basic discourse on modern understanding of and new methodology for identifying types of allergenic responses and food allergies; an interim report of data on eight patients observed in the Conners-Goyette study from the University of Pittsburgh; clinical observations and protocols under development; investigations at the University of Utah; protocols of studies projected at the University of Wisconsin, Harvard University and in Minnesota. Studies in two experimental animal models were presented and their potential usefulness as screening or evaluation techniques discussed. Against this background, members of the Advisory Committee have reviewed and further assessed a variety of points identified during the workshop. This report summarizes the present views of the Advisory Committee and indicates its recommendations for further studies.

The Nature of Hyperkinesis

The terms "hyperactivity, hyperkinesis and hyperkinetic syndrome" have been loosely employed in both lay and professional writings. Strictly speaking, hyperactivity is one of the symptoms of the hyperkinetic syndrome. Frequently, the latter term is mistakenly used interchangeably with that of the syndrome of "minimal brain dysfunction," which syndrome is of itself ill-defined. Indeed, Strother (3) has opined that "greater attention should be paid to classifying the very heterogeneous group of children now included under this rubric into more specific and homogeneous categories." There is no agreement—and little good evidence—as to the extent to which several seemingly related syndromes overlap. Definitive separation of these conditions has not been made in the writings of most physicians, behavioral scientists, or educators, including Dr. Feingold.

In an effort to clarify "the murky realm of nosology" P. H. Wender (4) notes that there is evidence for several etiological subgroups, and that the "hyperkinetic behavior syndrome" includes a number of clinical features: hyperactivity; short attention span and poor powers of concentration; impulsivity and the inability to delay gratification. There is diminished ability to experience pleasure and frequent refractoriness to disciplinary measures of any sort. Variably affected are perceptual-cognitive functions and neurologic function and coordination. These problems produce significant school underachievement in most children with the disorder. In school it contributes to classroom disruption; at home it is disruptive to family relations. Estimates of its incidence in U.S. schools range widely, frequently from 3 to 10%. Feingold (1) quotes some estimates as high as 25% or more of all children in certain schools. Others estimate a similar percentage of children as receiving drugs for the disorder (5). These variations reflect the inappropriate equating of different conditions "under the rubric of learning disabilities (i.e., hyperkinesis and reading retardation)" as well as other influences (6).

The origin and development of the disorders have not been established. Indeed, it is not even certain whether this is a discreet illness or a syndrome of many causes. There is evidence to support the hypothesis that some minimal brain dysfunction is genetically determined, produced by subtle central nervous dysfunction of biochemical nature (4). It is also hypothesized that some minimal brain damage may result from intrauterine factors or from difficult birth process (7). In rare instances low level lead enclephalopathy may contribute to such a syndrome, if one can extrapolate from experimental animal models (8, 9).

The lack of clarity in regard to these conditions is emphasized by the statement of The Council on Child Health of the American Academy of Pediatrics (10):

> "One must be cognizant of the fact that there is probably more confusion in relation to diagnosis and appropriate criteria for the use of medication for the treatment of hyperkinetic children than there is regarding the actual medication. Many physicians, as well as the general public, do not truly appreciate the differential diagnosis of the overactive child. It may be the result of basic personality, anxiety, subclinical seizure disorders, strictly in the eyes of the beholder, or true hyperkinesis; the latter is the only condition in which stimulants might be expected to be beneficial."

The Council on Child Health of the American Academy of Pediatrics (10) further notes that:

> "The hyperkinetic child is typically one of normal intelligence who fails to learn at a normal rate even though he is given the same educational opportunities as children with equal intelligence. He usually exhibits to some degree (1) short attention span, (2) easy distractibility, (3) impulsive behavior, and (4) overactivity. Although other behaviors ofttimes are seen in children with normal intelligence and academic lag, stimulant drugs seem to be most effective in the four behaviors just mentioned. Little is known about the effect of stimulant drugs on such things as poor motor integration, deficits in the perception of space, form, movement and time, and disorders of language or symbol development."

Response to drug therapy is unequivocal when it occurs and after satisfactory response to short term treatment, omission of the drug is immediately evident to those around the child, because he rapidly returns to the base line abnormal behavior (10). After long periods of control, discontinuance of drug therapy may be followed by remission in some 25% of patients. It is the practice of "many clinicians [to] discontinue the use of medication over each long school vacation; this allows the child to start a new year without medication. The medication is resumed only if the syndrome that initiated the original treatment hinders satisfactory school progress" (10).

There is little reliable information about the prognosis or natural course of hyperkinesis, how long the average child may benefit from medication, or whether taking stimulant drugs alters the ultimate prognosis in a substantial way. As an example, in a study recently published (11) in JAMA, data were summarized on 42 children, 13 of whom had been followed for two years, and 29 for one year. The subjects had been part of a double blind placebo study on the effect of different dose levels of Ritalin on behavior and school performance and were tested at one month intervals. Thus the population employed were known to be Ritalin responsive.

Twenty-six per cent of those taken off medication exhibited no deterioration of performance. This observation is important to interpretation of any studies of the effect of newly instituted regimens because the previously occurring symptoms do not always return immediately when medication is discontinued.

In a study at the University of North Carolina designed quantitatively to measure the motor activity and interest span of children diagnosed as hyperkinetic, Dr. Routh (12) reported that of 78 referrals from physicians, teachers and parents, 47% of the children were judged to be overactive and 53% were not. This, despite the fact that all of the children were considered to be "problem children" by those referring them to the testing service. Difficulties are inherent in all measurement techniques. Behavior perceived as hyperactivity may be more accurately described as non-goal directed activity. There is a sub-group of children with many of the other characteristics of minimal brain dysfunction who are in fact hypoactive.

Examples are numerous to illustrate the inconsistencies in rating of a child's activity by observers with different relationships to the subject, i.e., mothers, fathers, teachers, physicians, independent observers. Differences in perception by the observer do not follow a consistent pattern determined by the relationship to the child. For example, in a study in Iowa of teacher ratings of hyperactivity, it was found that older age teachers rated more children hyperactive than did young teachers (13).

Clinical experience indicates that many factors alter the activity patterns of such children or the perception of them by parents. Such factors range from the presence or absence of breakfast, weather conditions and resultant seasonal cycles that alter activities during cold seasons, to the interpersonal family relationships or existence of disruptive family problems. Age of the child appears to be another determinant of detection of the syndrome of hyperactivity. The majority of cases are noted at about the age of entry to school and there usually is a gradual diminution in the hyperactivity approximately at puberty or slightly thereafter. While some observers cite isolated cases of identifiable hyperkinesis in older individuals, this not the usual pattern. The syndrome is not recognized as a problem by school authorities in some areas of the world—again an example of differences in perception or of occurrence.

The diagnosis of hyperkinesis depends primarily upon the trained clinician's judgment, based upon history and observation of behavior. Some studies have employed trained classroom observers to help confirm the diagnosis. Again, behaviors which can be objectively measured may not adequately reflect the kind of problems that different children have. Objective measures of attention span have been developed (usually continuous performance tasks) and have been employed in making the diagnosis in some studies. Standard questionnaires completed by parents and teachers and involving observations at several different points in time provide useful evaluatory techniques.

The Feingold Hypothesis

In June 1973, Dr. Ben Feingold, a pediatric allergist from San Francisco, orally presented a preliminary report (14) in which he stated that hyperkinesis was associated with the ingestion of salicylates, of compounds which cross-reacted in the body with salicylates, and with common food additives.* This presentation was followed by a signed editorial in October, 1973 (1). The October 30, 1973 Congressional Record (16) contained the text of a paper given by Dr. Feingold at a meeting in London the month before and an account by a writer for the *Washington Post*. Dr. Feingold's paper printed in the Congressional Record yielded calls for the elimination of "food additives" from school lunch programs. He later restated his position in a book (2) entitled,

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[*] The term "food additive" is of itself a broadly encompassing one which is too often loosely used. The Food Protection Committee of the Food and Nutrition Board, National Academy of Sciences/National Research Council defines food additives (15) as "a substance or a mixture of substances, other than a basic foodstuff, that is present in a food as a result of any aspect of production, processing, storage or packaging. The term does not include chance contaminants." It does embrace such diverse substances as many essential nutrients (vitamins, minerals), flavoring agents (naturally occurring or synthetic), functional ingredients, preservatives and antioxidants (naturally occurring or synthetic), etc.

The U.S. Food and Drug Administration has defined "food additive" as: "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or

Why Your Child is Hyperactive. This book not only advocates the hypothesis, but also describes his dietary method of treatment. The presentation and the publication of the book have attracted a great deal of publicity. It has resulted in hundreds of letters to pediatricians, especially from parents seeking assistance, and although Dr. Feingold advocates his diet under medical management, it probably will lead to self-treatment programs.

Dr. Feingold currently advocates that a special label, identifying foods "without additives," be made available to be placed on all foods sold to the American public. By implication, of course, foods not so labeled would be considered by the interested consumer to contain "synthetic" additives.*

Dr. Feingold has not presented a specifically focused hypothesis. He depends upon the empirical observations he has made with patients under his therapeutic regime and on his special diet. He has reported that his management regime and an elimination diet (the Kaiser-Permanente or K-P diet), which was designed to be low in salicylates and free of "food additives," effectively treats 48% of the children presented to him with hyperkinesis. Of the children who respond, under his guidance, about ⅔ do so dramatically; the other third "favorably." It is important to note that Dr. Feingold claims (2) a response in *only half* of the children treated and dramatic response in but ⅔ of these. Thus his percentage of success is of the same magnitude that occurs following cessation of drug therapy (11).

Although Dr. Feingold's claims may prove valid, and, if so, may represent a major breakthrough in the treatment of this complex condition, the fact remains that his hypothesis is subject to serious criticism on several grounds. Of especially critical significance is the fact that no double blind controlled experiments have been conducted which permit the conclusion that dietary constituents are the critical variables. His observations, therefore, have served as a basis for generating an hypothesis, but they are inadequate for rigorous testing of the hypothesis. They do not justify definitive conclusions.

holding food; and including any source of radiation intended for such use), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use."

The distinction between "naturally occurring" and "synthetic" is usually vague and often relates to origin, not identity of the compound or mixture. For example, chemically synthesized β-carotene, the precursor of vitamin A, is "synthetic" while the chemically identical material biologically present in the carrot is "natural." Similarly, a mixture of three or so synthetic chemical components of a natural flavoring agent is termed "synthetic," while the "natural" agent contains these same components plus an additional number of compounds. Thus, the separation into "natural" and "synthetic" *per se* has no biological significance.

According to the Feingold regimen, not only the children, but their entire families are placed on the diet and regimen in order to ensure compliance. Parents are instructed to spend Saturday mornings making additive-free candy and cake with their children. There can be no question but that the total regimen significantly alters the structure and dynamics of the families by the introduction of the diet and its restrictions upon the child and his family. Since in many children hyperactive behavior is associated with family problems, it is quite possible that the alterations in the family dynamics may be causally related to the reported improvement in the child. Second, hyperactive behavior and its rating on a severity score are both subject to suggestibility. Dr. Feingold is charismatic and certain of the value of his program. It is possible that the confident expectations generated in the patient and the family affects the syndrome itself or at least the parents' ratings of the altered severity of the behavioral pattern. Third, parents or teachers who rate the children know that they are on the diet and this knowledge may influence their ratings. Fourth, objective rating scales like that developed by Dr. Keith Conners (17) have not been systematically employed to measure the parameters of the disorder or improvement. Dr. Feingold's improvement ratings are global, not specific.

The exact additive and nutrient content of the Feingold elimination diet remains difficult to assess. The proscriptions invoked may eliminate important and as yet unidentified food constituents. Knowledge of the chemical composition of foodstuffs is fragmentary. A number of common sources of important nutrients are proscribed, making it especially important that careful planning and food selection pertain to assure that nutrient requirements are met for any long term period of restriction to the regimen. Development of information on nutrients supplied by the regimen are currently underway in order to evaluate dietary patterns under the restrictions imposed and to determine if they may meet the long term nutrient needs of children. Until this question is answered, the committee feels that this regimen should not be used without competent medical supervision.

The initial rationale of the elimination diet advocated by Dr. Feingold was to avoid salicylate and salicylate-like compounds which occur naturally or as a result of processing. Data upon the naturally occurring salicylate compounds are notably incomplete and the dietary plan is based upon studies utilizing old and less-than-definitive methodology. The K-P diet calls for elimination of many commonly eaten members of the widest variety of food classes, with and without food additives, of all categories. There is *no* identifiable single substance or group of substances which the diet specifically removes and to the absence of which any observed effect might be attributed. The validity of this assessment by the Committee is indicated by Dr. Feingold's shift of emphasis from a suspected role of salicylates, aspirin-like compounds, to other food ingredients. It is noteworthy also that the K-P regimen (2) proscribes a wide variety of sundry items including over-the-counter medications, toothpastes and tooth powder, mouthwashes, cough drops, throat lozenges, antacid tablets and perfumes. Accordingly, the regimen markedly modifies other ingestibles as well as food.

A review (18) of the preliminary studies on eight patients by the Pittsburgh group studied in relation to the K-P regimen revealed that the majority of those subjects were judged by the parents to have exhibited improvement, sometimes continuously, regardless of which of two dietary regimens (the K-P diet or a "control") they were following. There were discrepancies, however, between the assessment by parents and by teachers of perceived behavioral changes in a portion of the studies and the teacher assessment was absent in a considerable number of the observational periods reported. Although the data were inconclusive, the preliminary results of the pilot studies were consistent with an interpretation of placebo effects and of variations in perception on the part of different observers, both of which are known to occur in studies of hyperkinesis.

Summary

The Committee concludes that data from critically designed and executed studies, free of the deficiencies of design noted, must be available before firm conclusions can be reached on the Feingold hypothesis. Accordingly, the Committee has considered at length the experimental design characteristics necessary to obtain definitive, interpretable data which may permit a decisive interpretation.

Guidelines for Experimental Design

While a variable number of experimental approaches may contribute to resolution of these complex questions, certain approaches will be more informative and feasible than others. The possibility of producing a wide variety of dietary products in identical pairs containing, or free of, specific chemical ingredients and indistinguishable to the consumer was considered. To execute effectively a program utilizing many such foods and to maintain the regimen as a complete double blind study would involve an enormous expenditure. On the other hand, the utilization of alternate dietary plans, i.e., the K-P diet and a "control," even when randomly administered, precludes strict double blind testing and introduces the variable placebo effect.

Patient compliance is difficult to control and monitor and might most easily be assured in a totally institutional or residential population. Potential methods for controlling compliance might be detection of metabolites or a marker in urine, but committee members are doubtful that appropriate technology may be available for such monitoring. This is being explored.

In order adequately to test the Feingold hypothesis, it is desirable that an "exclusion" diet planned for nutritional adequacy and in keeping with the K-P proscriptions be designed and utilized. Strong preference was expressed by the Committee that in a home setting there be used but one diet, i.e., no "control diets," because of anticipated difficulties in assuring compliance and the impossibility of avoiding the placebo effect. The use of a control diet would be more acceptable in a residential or institutional setting.

In any study it is essential to establish a valid behavioral base line before any manipulation is tried. The multiple and manifold nature of symptoms make it mandatory that the base line be established by having more than a single point and a *minimum* of two observations are required. The observations and evaluations should include assessments by the same observers in at least two different points in time and the observers should be the same as those who will subsequently assess the patient's behavioral pattern during the remainder of the study.

It was agreed that, after establishment of the behavioral base line and institution of the dietary regimen, a well designed double blind study utilizing, as a test or challenge, conventional foods prepared to be free of, or to contain, a single challenge ingredient or group of ingredients, would be most informative. The "challenge foods" should be made available for daily consumption by all members of the family. Such foods are more acceptable than capsules and the Committee recommends that at least two forms be developed. Each of these forms should be prepared in separate lots, one free of challenge material and another containing the challenge substance(s). They should be packaged in such manner as to preserve the double blind nature of the observations. Sequentially identified individual units should be packaged for consumption by the family, utilizing randomization and an unindicated code.

Behavioral observations of subjects will be made throughout the course of the experiment and only upon conclusion of individual studies will the challenge code be broken. In the event of adverse somatic reactions or deterioration of behavior, of course, the eating of the "challenge food" may be interdicted. A direct comparison of observed behavioral patterns with consumption or non-consumption of the "challenge substance" will permit definitive conclusions. These studies demand adequate independent monitoring and an appropriate number of participating families with hyperkinetic children.

The Committee emphasizes the necessity for utilization of quantitative base line measurements of behavior and of behavioral changes. As a minimum it is agreed that the Conners scale should be adopted and that assessments should be made by the use of independent (non-parent, non-teacher) classroom observers (such as graduate students in psychology) as well as by teachers and parents. In addition, there should be a clinical assessment by a physician at the beginning of the experiment and at least at monthly intervals throughout and additional measurements as feasible within the resources of the research team.

At least two weeks of base line data are recommended, the exact circumstances of which will depend upon the prior treatment (medication, diet or none), if any, of the patient. The frequency and quantity of observations during the base line period and the experimental periods should be such as to assure adequate assessment of individual variations. The reliability of all observations, including the initial observation, should be maximized by having the same observers rate the child throughout. Because of the known effect of medication on the symptoms being observed, the Committee felt that whenever possible any study should include a significant preliminary period of approximately two weeks during which there is no medication. It was agreed it would be advisable for at least one study to evaluate children who had never received drug medication. The period of observation following the base line should be a minimum of one month for the diet.

The code for the challenge materials should not be broken until the study is completed and the behavioral data are available for direct comparison with the data on the consumption of the challenge or control food. The advantage of the proposed approach is that interdiction is possible at any point simply by stopping the "challenge food." Careful records should be maintained of all such instances.

Ethical Considerations

The question of ethical acceptability of such studies has been carefully considered and the Committee agrees upon the following points:

The subject and the family will benefit from participation in such experiments whether:

(a) a challenge material can be incriminated, and thereby the opportunity of avoidance of a specific offending material results; or

(b) there is confirmed in a well controlled setting the value of the restricted diet as opposed to other factors; or

(c) no benefit occurs and thereby a troublesome exclusion diet of indefinite duration is avoided.

Interdiction of challenge feeding may occur at any point it is considered to be indicated. Dr. Feingold reports that there is rapid recovery (upon re-establishing his regimen) from the exacerbations that children on his regimen experience upon breaking of compliance.

Experimental Animal Models

Appropriate experimental animal models would seem to offer a potentially useful method for study of the possible relationships of foods and food ingredients to behavioral abnormalities and particularly promising for screening for any such effects. Accordingly, the Committee has reviewed three examples of promising models.

Rats made anoxic at birth with carbon monoxide later manifest hyperkinetic activity (19) which subsequently disappears upon maturation. The phenomenon is similar to that observed in human hyperkinesis.

In other studies, rats receiving low doses of lead during the neonatal period, subsequently develop hyperkinetic activity (9) and these animals respond to drugs in a manner similar to hyperkinetic children. For example, decreased activity occurred when the animals received amphetamine or methylphenidate in contrast to the stimulant effects of these drugs in normal rats. Also, they exhibit increased activity when given sedative doses of phenobarbital. This model system appears to offer a very promising experimental test for the screening of potential therapeutic agents.

Another potential experimental model is the production in developing rats of a syndrome caused by the administration of 6 hydroxy dopamine (6-OHDA) to five day old rat pups (20). This results in destruction of nerve terminals and depletion of brain dopamine to 38% of that of controls. During the first two weeks of post-natal life, the treated pups and littermate controls show little difference in spontaneous movement, but between 2-3 weeks of age, activity dramatically increases, to decline by the 4th week. The altered activity is associated with reduction of brain dopamine concentrations below the level of the normal controls.

These are examples of potential models that offer an opportunity for further study, not only of screening techniques, but also the possibility for elaboration of the mechanism of hyperkinesis.

Needed Funding

The Committee has reviewed funding needed to institute and complete currently projected studies, the protocols of which appear to be most promising of interpretable definitive results. The majority of these studies are in humans, but the estimates include modest funding for initiation of projects utilizing animal models. The Committee estimates that a total investment of $400,000—$500,000 is required. It is hoped that these funds may be obtained from a number of sources and that their utilization may be coordinated within the framework of the guidelines identified by the Advisory Committee.

Potential sources, in addition to the food and food related industries, logically would appear to be the Food and Drug Administration, National Institute of Education, National Institutes of Health, the National Science Foundation and other foundations. The role of The Nutrition Foundation would appear to be two-fold: a) the continuing support of the Advisory Committee for purposes of assessing and coordinating research program activities and evaluating overall developments and, b) direct support of recommended grants utilizing funds available from a variety of sources. Industry as well as other support for these activities could well be coordinated through administration by The Nutrition Foundation.

The most economical and expeditious initial test of the hypothesis would be to determine, in keeping with the requisite design, the behavioral response to "challenge foods" of known hyperkinetic children currently maintained on the K-P regimen. Dr. Ben Feingold has agreed to cooperate with the Advisory Committee in exploring such an initial study of patients in his series. Other cooperative centers of investigatory work are being explored.

Development of Challenge Food Vehicle

A task force from industry participated in by the staff of The Nutrition Foundation has, during the period beginning from the January 1975 meeting of the Advisory Committee, undertaken the preparation of appropriate challenge and placebo vehicles as recommended by the Advisory Committee. It is anticipated that these coded materials will be ready for utilization by investigators during the spring of 1975.

REFERENCES

1) Feingold, B. F. "Food Additives and Child Development," signed editorial in Hospital Practice, p. 11 (October) 1973.

2) Feingold, B. F. *Why Your Child Is Hyperactive*. Random House, New York, p. 212, 1975.

3) Strother, C. R. "Minimal Cerebral Dysfunction: A Historical Overview," Ann. N.Y. Acad. Sci. **205,** 6 (Feb. 28) 1973.

4) Wender, P. H. "Some Speculations Concerning a Possible Biochemical Basis of Minimal Brain Dysfunction," Ann. N.Y. Acad. Sci. **205,** 18 (Feb. 28) 1973.

5) Sprague, R. L. and Sleator, E. K. "The Effects of Psychopharmacologic Agents on Learning Disorders," Pediatric Clinics of North America **20,** 719, 1973.

6) Minskoff, J. G. "Differential Approaches to Prevalence Estimates of Learning Disabilities," Ann. N.Y. Acad. Sci. **205,** 139 (Feb. 28) 1973.

7) Kalverboer, A. F., Touwen, B. C. L. and Prechtl, H. F. R. "Follow-up of Infants at Risk of Minor Brain Dysfunction," Ann. N.Y. Acad. Sci. **205,** 173 (Feb. 28) 1973.

8) David, O. J. "Association Between Lower Level Lead Concentrations and Hyperactivity in Children," Environmental Health Perspectives **7,** 17 (May) 1974.

9) Silbergeld, E. K. and Goldbert, A. M. "Hyperactivity: A Lead-Induced Behavior Disorder," Environmental Health Perspectives **7,** 17 (May) 1974.

10) Council on Child Health of the American Academy of Pediatrics. "Medication for Hyperactive Children," Pediatrics **55,** 560 (April) 1975.

11) Sleator, E. K., Sprague, R. L. and von Neumann, A. "Hyperactive Children. A Continuous Long-Term Placebo-Controlled Follow Up," JAMA **229,** 316 (July 15) 1974.

12) Routh, D. "The Clinical Significance of Open-field Activity in Children," Pediatric Psychology **3,** 3, 1975.

13) Johnson, C., University of Iowa, personal communication, 1974.

14) Feingold, B. F., German, D. F., Braham, R. M. and Simmers, E. "Adverse Reaction to Food Additives," AMA Annual Convention, New York, 1973.

15) Committee on Food Protection, Food and Nutrition Board, *The Use of Chemicals in Food Production, Processing, Storage, and Distribution*, National Academy of Sciences, Washington, D.C., p. 34, 1973.

16) Beall, Senator J. G., "Food Additives and Hyperactivity in Children," Congressional Record, S 19736, October 30, 1973.

17) Conners, C. K. "Psychological Assessment of Children with Minimal Brain Dysfunction," Ann. N.Y. Acad. Sci. **205,** 283 (Feb. 28) 1973.

18) Goyette, C. Personal communication to the National Advisory Committee on Hyperkinesis and Food Additives, January 1975.

19) Culver, B. W. and Norton, S. "Reversible Hyperactivity in Young Rats After Single Exposure to Carbon Monoxide," Pharmacologist **16,** 208, 1974.

20) Shaywitz, B. A. "Selective Brain Dopamine Depletion in Developing Rats: An Experimental Model of Minimal Brain Dysfunction," Personal communication, 1975.

Appendix

MEETING OF THE NATIONAL ADVISORY COMMITTEE ON HYPERKINESIS AND FOOD ADDITIVES

Glen Cove, New York
January 12-14, 1975

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March 28, 1974

CRITIQUE OF MANUSCRIPT BY BEN F. FEINGOLD, M.D.
ENTITLED
"ADVERSE REACTIONS TO FOOD ADDITIVES"

The following individuals were brought together under the auspices of the Grocery Manufacturers of America, Inc. (GMA) to jointly evaluate and prepare this critique:

Leon Golberg, D.Sc., D.Phil., M.D., Albany Medical College
Richard L. Hall, Ph.D., McCormick & Company, Inc.
Robert W. Harkins, Ph.D., GMA
Channing H. Lushbough, Ph.D., The Rockefeller University
Gerald Solomons, M.D., University of Iowa

Participating but unable to attend the meeting was David E. Schecter, M.D., of the Albert Einstein College of Medicine and the William Alanson White Institute of Psychiatry.

SUMMARY

We have examined the manuscript entitled "Adverse Reactions to Food Additives With Special Reference to Hyperkinesis and Learning Difficulty (H-LD)" as prepared by Dr. Ben F. Feingold and published in the Congressional Record of October 30, 1973 (S.19736-19742). Because of a number of serious deficiencies in the experimental design and/or in the reporting of clinical observations in this manuscript, plus the availability of information and reasoning pointing in other directions, we find almost wholly without support the hypothesis put forward by Dr. Feingold that food additives are linked to H-LD. At the same time, one cannot state categorically that there is no relationship between ingestion of food additives and hyperkinesis and learning disorders.

The Feingold manuscript asserts that there is a relationship; this relationship has not been scientifically demonstrated. The design of a rigorous study to evaluate this concept is compatible with the continuing need to assure that every precaution is taken to protect the public health.

SPECIFIC COMMENTS ON THE MANUSCRIPT

Prevalence of Disorder

Hyperkinesis or hyperactivity is predominantly an American syndrome. While it has been reported in other cultures and in other countries, the incidence of reporting is much higher in the United States than elsewhere. Although the incidence of reporting has increased in recent years, we question whether the incidence of hyperkinesis has, in fact, changed during the last few decades. Hyperkinesis is primarily an affliction of boys rather than girls, and it seems unlikely that the incidence of this disorder could approach the average values of "20 to 25 percent and in some cases 40 percent of the entire school population." However, it is possible that the reporting of hyperactivity could approach these values. One should not confuse the level of reporting with the incidence of the condition.

MacKeith (Pediatrics, 49: 325, 1972) commented on the incidence of hyperkinetic children in the Isle of Wight Survey. In this study, only nine children in a population of 2,326 were diagnosed as having a hyperkinetic syndrome, an incidence of less than four-tenths of one percent.

Symptomatology

Many disciplines are involved in the assessment of the hyperkinetic child. Parent groups, physicians, and educators have been bombarded with professional and lay articles describing the condition and its treatment. This has brought about a dramatic increase in the use of psychostimulants to manage these children. The recent practice of certain firms to promote pharmaceutical products to educators may have increased the pressure for the physician to prescribe medication, as many referrals are initiated by teachers. From such efforts have come popularized labels and sometimes an easy out for the management of "problem" children.

In the last decade, hyperkinesis and hyperactivity have become popularly accepted as authentic and common disorders. Because of the wide range of symptomatology reported as manifestations of hyperkinesis, it is possible to include virtually any child from day to day. Within the broad sweep of its definition, a list of some typical symptoms is shown below:

At Home

(1) Cannot remain still
(2) Cannot conform to limits or prohibitions
(3) Makes excessive demands
(4) Has sleeping problems
(5) Shows unwarranted aggression
(6) Is a general pest

At School

(1) Is talkative
(2) Fidgets continuously
(3) Cannot concentrate
(4) Has short attention span
(5) Cannot conform to limits or prohibitions
(6) Shows poor school achievement

Relationship with Other Children

(1) Cannot make friends
(2) Fights without provocation
(3) Has poor manners
(4) Is extremely bossy
(5) Disregards rights of others
(6) Is continually rejected

In Dr. Feingold's manuscript, the following characteristics of the clinical pattern are described:

(1) Marked hyperactivity
(2) Short attention span -- jumps from one activity to another
(3) Fidgetiness
(4) Irritable -- overly sensitive
(5) Unpredictable and unmanageable
(6) Quick-tempered, explosive and panics easily
(7) Low tolerance for failure and frustration
(8) Exceptionally clumsy -- poor coordination; eyes and hands do not function well together; has trouble buttoning
(9) Has difficulty drawing and writing
(10) Cannot seem to keep from touching everything and everyone around
(11) Normal or high IQ but fails at school

Obviously, behavioral manifestations such as those described are highly subjective. These manifestations should not be confused with clinical signs which can be objectively evaluated by a physician. Thus, a child may be deemed to be hyperkinetic by one observer--perhaps a parent or teacher--and deemed normal by a second observer. Since evaluation of the manifestations is so subjective, improvement in these manifestations must be rigorously evaluated by more than one observer.

Solomons (Annals N.Y. Acad. Sci., 205: 335, 1973) recently commented on the unreliability of parents in reporting the behavior and activity level of their children. Studies have shown little agreement between the parents, and they are unable to provide objective information concerning the maladaptive behavior of their own children. Unfortunately, even a teacher is not always able to be objective in evaluating a problem child Because of the looseness of definition of the behaviors which are used as diagnostic criteria to classify a child as hyperkinetic, the reliability of teachers' evaluations is generally low in many areas. Where a teacher's own salary progression and promotion are directly linked to class performance, there is an obvious temptation, not to say incentive, to get rid of troublesome pupils by relegating them to the hyperkinetic category that requires special treatment.

Patient Selection

The Feingold manuscript defines neither hyperkinesis and learning difficulty nor criteria for selecting the patients enrolled in this study. This lack of quantitative indices for enrollment and evaluation may undermine the conclusions of the study. Criteria for patient improvement are also unstated. Is improvement based on the parents' or teachers' evaluations? Is it based on clinical signs? We would suggest that patients enrolled in an experimental study to evaluate the effect of therapeutic intervention in hyperkinesis be evaluated by several trained, impartial observers. Those involved emotionally with the patient--parents, other relatives, teachers, etc.--are not able to evaluate objectively the progress of patients during intervention. Their opinions are useful as corroborative evidence, but should not be utilized as the primary criteria of treatment success or failure.

Although the manifestations of hyperkinesis are varied, we believe that the reporting, such as the case of a seven-year old boy who exhibited a trait of "charging oncoming cars with his bicycle," is not a sign of hyperkinesis but of emotional disturbance.

Experimental Design

The major deficiency in the manuscript is the absence of a control group. There is no way to determine whether the application of a salicylate-free diet was effective or ineffective. It is well known that the placebo effect in the management of hyperkinesis can be very large. In perhaps one of the best demonstrations of this effect, Knights and Hinton (J. Nerv. Mental Dis., 148: 643, 1969) demonstrated, according to one rating scale, that 88% of the patients receiving Ritalin improved. However, this value was nearly matched by 67% of the patients in the control group who received the placebo and also improved.

There is no indication in the manuscript of how many patients did improve on the salicylate-free diets. The manuscript suggests that the author was able to successfully manage "some" of the children. In a popularized news article, Morton Mintz (The Washington Post, October 29, 1973) reported that "Dr. Feingold said he had achieved 'dramatic results' with the special diet in 15 to 18 of 25 hyperkinetic children in his practice. Some of the children who did not improve did not stick to the diet, he said." We would like to know whether the number of children who improved on the diet was 15 (60%) or 18 (72%); whatever the accurate number may be, we would point out that the percentages are very similar to the 67% of the hyperkinetic children who improved while receiving the placebo in the study of Knights and Hinton.

Hyperkinesis and Learning Difficulty

Dr. Feingold has lumped hyperkinesis and learning difficulty into a single entity. We do not believe this is appropriate. We do not agree with the author's statement that "hyperkinesis and learning difficulty are commonly interlinked and are actually different aspects of an identical problem. This is particularly true of dyslexia, a generic term applied to a whole category of reading and spelling disabilities."

We would agree that hyperactivity and learning disorders are two facets of minimal brain dysfunction. However, we are unaware of documentation which would indicate that children with dyslexia are hyperactive, or that hyperactive children suffer from an innate learning disorder other than a non-specific, generalized, limited attention span. Decreased attention span, a characteristic of hyperactive children, may result in academic underachievement. If the hyperactivity can be moderated by environmental factors or by drugs, academic progress improves, frequently quite markedly. On the other hand, children with dyslexia are not generally responsive to psychostimulants.

To expand further the list of criteria of H-LD to include all children reading below grade level further weakens Dr. Feingold's thesis. There is no reference to the work of Eisenberg (Pediatrics, 37: 352, 1966) showing that 40 to 50% of the children in large urban areas are reading below grade level. Reading achievement and other academic skills are routinely linked to a variety of non-food factors. Those factors which have been correlated and for which there is a rational explanation include family income, availability of reading materials in the home, educational achievement of the parents, and teacher skills. In certain urban areas, inner city children will not meet national academic norms, while suburban children will meet and exceed the national norms. Although there is no evidence to prove that the ingestion of food additives is not related to inadequate academic skills, it is highly improbable that ingestion of food additives is a causative factor in reducing reading ability. The foods available for purchase, at least those offered by supermarket chains, are essentially similar throughout a metropolitan area. While consumption patterns vary among ethnic and economic groups, we suggest that the food patterns are more uniform throughout a metropolitan area than are other environmental factors, such as the educational achievements of the parents.

Salicylate-Free Diet

The recent article by Samter (Hospital Practice, December 1973, p. 85) appears to challenge the basis of the use of salicylate-free diet in the management of aspirin intolerance. Samter reports that the diverse expressions of aspirin intolerance--shock, rhinorrhea, nasal polyps, bronchial asthma, prolonged bleeding time--are caused by aspirin (acetylsalicylic acid), FD&C Yellow No. 5 (tartrazine), indomethacin (an indole derivative with antipyretic, analgesic, and anti-inflammatory properties), and aminopyrine (an antipyretic and analgesic). However, other compounds more closely related chemically to acetylsalicylic acid (e.g., sodium salicylate, propionyl salicylic acid, butyryl salicylic acid, caproyl salicylic acid, choline salicylate, thio-aspirin, and N-acetyl-p-aminophenol) had no untoward reactions when used as challenges to aspirin-intolerant patients.

Salicylates and Aspirin Intolerance

To the best of our knowledge, acetylsalicylic acid is not a naturally-occurring substance. The naturally-occurring salicylates would normally be hydrolyzed to the free salicylate radical prior to absorption. If sodium salicylate has no effect on aspirin-intolerant patients, what is the rationale for use of a salicylate-free diet? If the diet does indeed produce the results claimed for it, its effectiveness would not appear to be due to the reduction in the level of dietary salicylates per se. The effectiveness of dietary manipulations of both aspirin-intolerant and hyperkinetic patients requires further study.

The work of Samter (ibid.) suggests that "a small percentage of (aspirin-intolerant) patients" did respond to a challenge of tartrazine with intense broncho-obstructive symptoms. Apparently this reaction occurs only in those individuals with a pre-existing systemic disease. This disease state is not, as previously believed, an allergic response to aspirin. Samter includes the following classifications of aspirin-sensitive patients according to severity:

Mild

Slight cough
Rhinorrhea
Tension
Apprehension
Dyspnea
Nausea
Gastrointestinal upset

Moderate

Slow onset
Tightness in chest
Urticaria
Angioedema
Breath sounds decreased
Asthma resistant to usual therapy

Severe

Sudden onset
Tightness in chest
Acute bronchospasm
Cyanosis and dyspnea
Breath sounds decreased
Unconsciousness
Shock

Comparison of the clinical signs of aspirin-intolerance with the clinical observations of hyperkinesis or of learning disorders suggests no direct relationship. The rationale for the use of a salicylate-free diet, either for the management of aspirin intolerance or for hyperkinesis and learning disorders, is not clear.

From a nutritional and metabolic standpoint, one would not expect a salicylate-free diet to alleviate aspirin intolerance. Similarly, one would not expect fruits and vegetables, excluded from a salicylate-free diet, to be a causative agent in either aspirin sensitivity, hyperkinesis, or learning disorders.

Food Colors and Artificial and Nature-Identical Flavors

Dr. Feingold's manuscript states that:

> Of the various clinical patterns induced by the adverse reactions to artificial colors and flavors perhaps the most important and also the most dramatic are the behavioral disturbances in children.

There is no reference or support offered for this statement; apparently it is the opinion of the author. We know of no data which relate behavioral disturbances directly to the ingestion of food additives.

Dr. Feingold suggests that:

> Except for terminology, there is no difference between artificial colors, flavors, and many drugs. They are all low molecular weight chemicals.

This statement disregards much of modern biochemistry which has revealed the relationships between the detailed chemical structure of substances and their physiological effects as nutrients, drugs or inert or hazardous substances. It should be stressed that the human body functions to a large degree by means of low molecular weight chemicals. Our existence depends on intermediary metabolism, which involves such chemicals. Furthermore, a considerable proportion of the natural components of food comprises low molecular weight chemicals. Hence, Dr. Feingold's reference to a special category of "low molecular weight chemicals" composed of food additives and drugs lacks scientific justification.

The statement has other implications which need examination in some detail. Dr. Feingold presumably considers "artificial colors, flavors, and many drugs" as being (a) synthetic and (b) not found in nature. If this is his argument, not only is it largely incorrect, but so also are some of its further implications.

Currently, there are only eight man-made colors permitted for general use in foods: FD&C colors identified as Green 3, Yellows 5 and 6, Reds 2, 3 and 40, and Blues 1 and 2. (Note: The Feingold manuscript incorrectly lists Violet 1 and does not include Red 2.) Three other synthetic colors are permitted for limited use: Citrus Red No. 2, use limited to coloring the skins of oranges; Orange B, use limited to coloring the casings or surfaces of frankfurters and sausages; and Red No. 4, use limited to coloring maraschino cherries.

Each of these synthetic colors has undergone intensive toxicological evaluation, including acute and chronic toxicity testing. In 1971 the Food and Drug Administration ordered that each of the generally-used colors subject to ingestion must also undergo teratology and multi-generation reproduction tests. These studies are nearing completion with many of the test results already forwarded to the FDA. The synthetic colors have had perhaps the most rigorous testing ever required of any such class of food additives, with the possible exception of the artificial sweeteners. Much of this testing was conducted by the Toxicology Division of FDA. When used in foods, colors are permitted at levels well below the "no-adverse-effect" levels determined from the animal feeding studies. The use of synthetic food colors was evaluated by the Committee on Food Protection of the National Research Council ("Food Colors," National Academy of Sciences, 1971), and has been the subject of several reports by the Joint FAO/WHO Expert Committee on Food Additives.

In contrast to the synthetic colors, there are 25 natural coloring substances derived from natural sources. These substances are permitted to be added to foods because they are "generally recognized as safe" under the conditions of use. By and large, these natural materials have not been subject to toxicological evaluation. Legislators and regulators have assumed that apparent lack of adverse effects from human experience with naturally-occurring substances tends toward a conclusion of safety. While this can be a useful consideration in safety evaluation when taken together with other evidence, it does not boil down to a simple conclusion that "natural is safer than synthetic." In fact, the synthetic parts of our diet are much better identified, more extensively studied, and by every indication, consumed with a wider margin of safety than the natural components (Chemicals and Health, Report of the Panel on Chemicals and Health of the President's Science Advisory Committee, September 1973, p. 68).

Synthetic colors are widely used in processed foods because of their uniformity, high tinctorial qualities, and availability. Natural colors are less uniform, vary from batch to batch, have less tinctorial strength, and are limited in their availability. The situation for natural flavors is not unlike that for natural colors. Both economic and technological factors have required suppliers of flavors to synthesize many flavoring materials. However, in contrast to synthetic colors, most synthesized flavor ingredients are identical with the naturally-occurring substances responsible for the same flavors in foods. While "synthetic," they are nature-identical. For very many such synthesized but nature-identical flavor ingredients, our intake from a variety of natural food sources is much larger than our intake resulting from intentional use. There is no reason to believe that a nature-identical flavor synthesized by man could cause untoward reactions in man simply because it was created in a laboratory rather than by a plant. Indeed, the enormous number of components in natural products, many not yet identified, suggests the opposite. When placed in the context of nature-identical, the suggestion by Dr. Feingold that "there is no synthetic product (flavor) that can not be detected by an individual with a very acute sense of taste" loses all meaning.

To the best of our knowledge, at the levels used in food neither the synthetic colors nor the flavors, both nature-identical and synthetic, exercise any pharmacological effects, except when huge doses are administered to animals. It is, of course, impossible to exclude the possibility of very rare adverse reactions to any substance, natural or synthetic.

Alternative Explanations

Among many other explanations that have been put forward for the causation of hyperkinesis, attention should be drawn to lead ingestion and/or inhalation of airborne lead. The etiological role of lead in hyperkinesis has been strongly supported by the Environmental Protection Agency on the basis of evidence which, while still only suggestive, is far stronger than that of Dr. Feingold (EPA-NIEHS Conference on Low-Level Lead Toxicity, October 1-2, 1973, Raleigh, N.C. Proceedings to be published in "Environmental Health Perspectives," 1974). Of course, any part played by lead in causing hyperkinesis does not exclude the possibility of a contribution to the same end-result brought about by food additive ingestion; but the need for control groups in any study design is clear.

We have already commented that several aspects of hyperkinesis or behavioral problems assumed to be hyperkinesis and their alleviation need both more rigorous and more extensive study. But some of what is known suggests other, probably more fruitful points of attack than additive ingestion. The large placebo effect is an indication of the heavy psychological components in these conditions. For many of Dr. Feingold's patients, a highly restricted diet was probably the first persistent regimen, or discipline, to which they had ever been subjected. From these observations follow some of the suggestions we urge if any further work in this direction is attempted.

RESEARCH NEEDS

Before Dr. Feingold's hypothesis could receive general acceptance by the scientific community, it requires validation. As it is now reported, there is no way to prove (or disprove) his hypothesis that food colors or food flavors are causative agents in hyperkinesis or learning disorders without much additional data. Certainly the current manuscript falls far short of demonstrating a causal relationship between colors and flavors and hyperkinesis, while there are alternative, and more probable, explanations of the observations he makes.

Research Design

In any future work in this direction, the clinical protocol should include the following:

(1) Objective signs for the selection and continuing evaluation of patients. If definitive clinical signs cannot be determined, patient progress should be monitored by at least three trained clinicians.

(2) Adequate patient follow-up is absolutely essential. Each patient should be evaluated at least monthly for the first three months and at regular intervals thereafter.

(3) The study should include at least four groups:

  (a) The intervention group with dietary modification,

  (b) A group similar to (a) with other dietary modifications not anticipated to be related to the omission of synthetic colors and flavors,

  (c) A control group with no intervention other than clinical monitoring, and

  (d) A control group with no dietary intervention but given a placebo drug.

(4) The study should be double-blind in construction. The patients should receive no instruction on the relative merits of either dietary modification. It is essential that those trained clinicians who evaluate the patients not know to which group the patient was assigned.

(5) After an appropriate period of time, perhaps four to six months, the children should be regrouped through a crossover design.

(6) The patients not responding to the experimental design should be evaluated for the effectiveness of psychostimulants.

(7) Dietary histories should be recorded for all patients accepted into the experimental design, and these intakes should be compared with those of an unaffected peer group. Through analyses, the dietary levels of salicylates and selected food additives should be measured on a regular basis.

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Statement before Senate Sub Committee on
Health, Senate Labor and Public Welfare
Committee and Administrative Practice and
Procedure, Senate Judiciary Committee

by

Frances W. Dickson
(Mrs. A. W. Dickson)

September 11, 1975

U. S. Senate, First Session, 94th Congress

Testimony of Frances W. Dickson

Mr. Chairman and Members of the Subcommittee:

I submit the following statement on my own behalf for your consideration. It is a plea for protection from artificial colors and flavors in foods.

One of my teenaged sons has suffered for years from hyperactivity. The other has had the same problem but to a lesser extent. Both boys have high I.Q.'s but short attention spans, associated with the hyperactivity, which have kept their grades below expectations.

After reading Dr. Ben F. Feingold's book, "Why Your Child Is Hyperactive," I put my children and myself on his recommended diet free of aspirin, to which we had been sensitive for years, natural salicylates such as tomatoes and oranges, and artificial food colors and flavors.

At that time my younger son was not only hyperactive in school and at home but was having spells of belligerency, destructiveness, crying and screaming, at times uncontrollably. Trying a diet free of so-called junk foods, a few fruits and vegetables seemed a small enough price to pay for a possible cure. Our pediatrician agreed.

I told my sons we were going on a diet that would help them gain weight and get rid of their mild acne, both conditions they badly wanted. I did not mention hyperactivity or Dr. Feingold's book. I wanted to see what if any changes would occur without the boys being unduly influenced.

The boys agreed to cooperate and I joined them in the diet. It wasn't easy. My sons had to give up all the foods boys seem to be made of _ hot dogs, pizza, most sandwich meats, egg noodles, spaghetti with tomato meat sauce, relish and ketchup for hamburgers, commercial chocolate products as hot cocoa and syrup for milk, to name a few.

But this was nothing to compare with the sweet and snack list of forbidden foods. Out went chewing gum , buttered popcorn, all but one soft drink- Seven-up, one brand of ice cream, one candy bar - German Sweet Chocolate, actually a baking chocolate, a few cookies and candies from Pepperidge Farm. (Since that time we have found a few more commercially prepared items which we may eat.)

I would like to point out that all of the forbidden foods mentioned above, save for the tomato dishes and pickle relish, were forbidden because of the possible or actual addition of artificial colors and flavors.

It soon became apparent that if we were to eat anything but the simplest diet of home cooked foods, I would have to do more cooking from "scratch." I raced home from my job as teacher to fill up the snack and cooky jars so the boys would not be tempted to go to the nearest store for forbidden ice cream and candies.

During the first week or so on the diet I felt things were calming down with the boys but I thought perhaps it was just a conincidence or maybe I was in a better mood. Three weeks passed, however, before I had any real evidence. The older son came in from delivering his morning papers to complain "I just can't go back to feeling like this" and added"I've been feeling so good for the last two or three weeks and now this."

I knew he had eaten supper at a friends the night before and had had two cola drinks and butter. I told him then about the diet and he agreed it would be worth it to stay on it. I was sure it was working, fo during the second week of the diet he had settled down to read 15 books and write a 12-page paper on the atom for tenth-grade chemistry. I had never seen him study for such long periods of time. He would work through meals, TV and other leisure activities with rarely a flare-up of temper or frustration.

The younger son began to have better days at school and at home. The fits of screaming and crying became fewer and less intense. He seemed more relaxed and congenial.

Most of the things I've said about my sons reactions I could say for myself. I had been aware that certain foods "bothered" me often in vague ways of just "not feeling right," heart palpitations and drastic swelling of the abdomen which lasted several hours. I was not aware of my mood changes until I went on the diet. These symptoms only appear now when I have eaten forbidden foods and additives.

The proof of this diet is in the homemade pudding. It it didn't work by making my children feel better, they would never stay on it so faithfully. It takes a lot of will power to turn down a friend's offer of a drink or candy bar, particularly when there is nothing else to eat.

We depend so much today on prepared foods and "mixes" and on commercial candies and drinks that one has to go to a great deal of effort to prepare food free of artificial additives for one day for a family. I know. I do it every day. Many mothers haven't the time, the know-how or patience for such a regimen. Our children increasingly have money and access to commercial foods and snacks. They are not usually prepared to make the choice between pure food and junk food. It seems to me we owe them and ourselves the protection of pure food at least until it has been proven the additives are not dangerous. Part of the protection involves making food free of these additives readily available in the form of snacks, drinks and prepared foods that we have come to depend on.

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Bethel, Connecticut

March 21, 1975

Dr. Keith Connors
NATIONAL INSTITUTE OF EDUCATION
Boston, Massachusetts

Dear Dr. Connors:

The article in the New York Times on February 9, 1975 has proved very rewarding to us.

We have a child who fits into the category of hyperkinetic and after reading the article, I purchased only foods which contained no artificial colors or artificial flavors. To make a long story short, last week after using only two weeks into the new diet, our child's teacher sent home a note stating she noticed a change in our son's behavior. We, too, have seen the change and needless to say, are ever so delighted.

We would like to ask you if there is a detailed sample diet which you offer as a basic diet to follow or is just the elimination of the mentioned foods in the article sufficient?

Our many, many thanks for the fine work you and Dr. Feingold are doing. It was good to hear these important facts on a New York radio station a few weeks ago.

Cordially,

Food Additives and Hyperkinesis: A Controlled Double-Blind Experiment

C. Keith Conners, Ph.D., Charles H. Goyette, Ph.D., Deborah A.
Southwick, M.S., James M. Lees, M.D. and Paul A. Andrulonis, M.D.
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Alan Cohen, M.D. and Janice Hubka, M.A. assisted during pilot phases of the program in Boston. Joanna Dwyer, D.Sc. was instrumental in providing much useful advice in the early phases of the study regarding dietary and design aspects of the investigation.

Benjamin Feingold, M.D. served as a consultant and advisor on the project, and of course provided the initial impetus to open up the entire field of investigation for study.

Food Additives and Hyperkinesis: A Controlled Double-Blind Experiment

C. Keith Conners, Ph.D., Charles H. Goyette, Ph.D., Deborah A. Southwick, M.S., James M. Lees, M.D. and Paul A. Andrulonis, M.D.

University of Pittsburgh Department of Psychiatry

Introduction. In June of 1973 a preliminary report was presented by Benjamin F. Feingold, M.D., professor emeritus of the Kaiser-Permanente department of allergy, in which it was proposed that hyperkinesis in childhood is associated with the ingestion of salicylates, of compounds which cross-react with salicylates, and with common "food additives", i.e. artificial flavors and colors. Other oral presentations, including a popular book and testimony in the Congressional Record, have served to popularize the hypothesis that this common childhood behavior disorder may be caused by artificial flavors and colors in food.

The medical literature shows that urticaria and asthma can be induced by food additives and dyes (Chafee & Settipane, 1967), and that strong allergic reactions occur to some dyes in patients with aspirin hypersensitivity (Juhlin, et. al., 1972). Feingold noted (1973) that an adult patient with aspirin hypersensitivity showed remission of psychiatric disturbances when the patient was placed on a diet free of natural salicylates, food colors and artificial flavors. Because of the supposed cross-reactivity of salicylates and dyes (especially tartrazine, the yellow FD&C #5 dye), Feingold treated hyperactive children with a diet free of so-called natural salicylates (found in many fruits) and all artificial colors and flavors.

A number of criticisms were immediately raised against Feingold's claims (many of these are summarized in the National Advisory Committee on Hyperkinesis and Food Additives Report to the Nutrition Foundation, based on a conference held in January, 1975). Included among the criticisms are that: (1) the patients reported upon were not described by any standard methods, nomenclature or measurements; (2) no controls were utilized to compare changes against those in the children treated with the elimination diet (hereinafter referred to as the K-P diet); (3) no objective measures of change were employed; (4) the observer of change was not blind to the treatment being evaluated and had a vested interest in confirming the hypothesis; (5) alternative explanations based on commonly accepted placebo phenomena were not considered; (6) no measures of the actual dietary habits of the patients were presented to rule out the possibility of unintended harmful dietary effects or that changes in the diet other than artificial flavors and colors could cause the effect; (7) claims of percentage improvement varied from one presentation to another, and no hard statistical numbers were ever employed. In short, the claims were strictly impressionistic, anecdotal, and lacking in objective evidence.

Because of the wide public interest aroused by the claims, however, and because of the public health implications of the hypothesis, the National Institute of Education (NIE), of the Department of Health, Education and Welfare (HEW), solicited contract proposals for the study of the hypothesis. An initial contract was awarded to the Human Resource Institute of Boston, with C. Keith Conners as Principal Investigator. Since the contract was awarded in May of 1974, only a small pilot study was completed before the end of the school year. In the subsequent October Dr. Conners took up a new position as Associate Professor at the University of Pittsburgh Medical School's Department of Psychiatry where the bulk of the present work was undertaken.

Method

Subjects. In order to be eligible for the study, children had to be between the ages of 6 years and 12 years and 11 months. The children were examined by a child psychiatrist who utilized a standardized examination and rating scale, and had to agree that the child fit the criteria for hyperkinetic reaction of childhood (308.0 of the APA DSM II) based upon the medical and social history, parent and teacher symptom ratings, and the psychiatric rating scale. Demographic, history, physical and mental status examination, neurologic evaluation and rating scales were all forms adopted by the National Institute of Mental Health Psychopharmacology Research Branch for conducting scientific trials in pediatric populations with drugs and related types of studies (Appendix I). The purpose of these instruments was to record in an objective and standardized manner the entire set of data available on each child.

Central to this study was the use of two symptom rating scales filled out by parents and teachers (Conners, 1969, 1970). The teacher scale is a 39-item list of common behavioral problems found in school age children. The parent scale is a 93-item symptom list covering a wide variety of behavioral reactions in children. Both scales have been demonstrated to have satisfactory reliability and validity. Most of the present report will deal with data from a 10-item subscale ("hyperkinesis index") which measures the cardinal symptoms of the hyperkinetic syndrome. The 10 items are identical for parents and teachers. Since each item is scored 0, 1, 2, or 3, scores may range from zero through 30. It should be emphasized that these scales do not diagnose hyperkinesis; diagnosis is a complex judgment based upon all of the data available to the clinician; but studies have shown that a cut-off score of 15 on the 10-item scale is an efficient discriminator between diagnosed patients and classroom controls (Sprague, et.al., 1975), and that the scale is sensitive to changes brought about by other therapies.

Table 1 shows that of 37 children referred for the study, 15 completed the entire program, with the other children largely having dropped out prior to the actual start of the experiment itself.

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Table 1 here

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In addition to symptoms of moderate to severe degree, the children had to have a history of at least two years duration of the major symptoms of the hyperkinetic syndrome. Most had in fact been seen as problems by parents from a relatively early age.[1] Table 2 shows the distribution of ages in the children completing this study, and Table 3 summarizes the selection criteria.

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Tables 2 and 3 here

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[1] A more complete description of the subject sample in terms of history, demographic status, physical characteristics and other details will be provided in a final report, based upon more complete analysis of the NIMH forms by the Biometrics Laboratory of George Washington University.

Table 1

FOOD ADDITIVES AND HYPERKINESIS SAMPLE FLOW SHEET

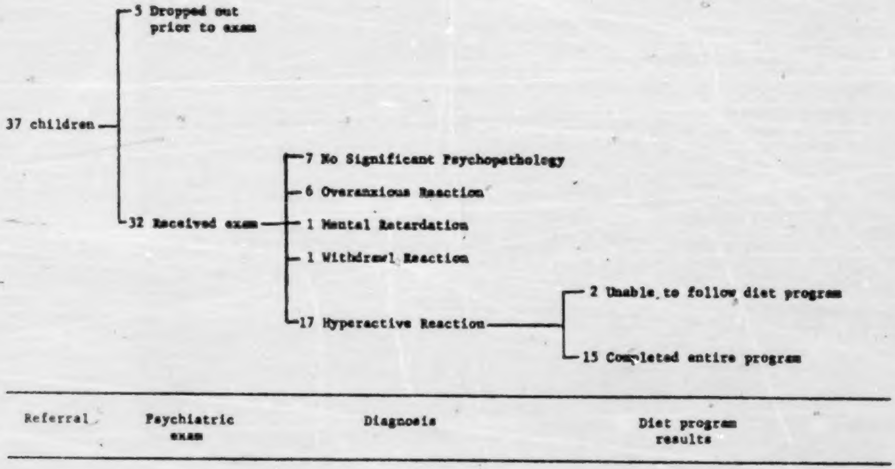

37 children
5 Dropped out prior to exam
32 Received exam
7 No Significant Psychopathology
6 Overanxious Reaction
1 Mental Retardation
1 Withdrawl Reaction
17 Hyperactive Reaction
2 Unable to follow diet program
15 Completed entire program
Referral
Psychiatric exam
Diagnosis
Diet program results

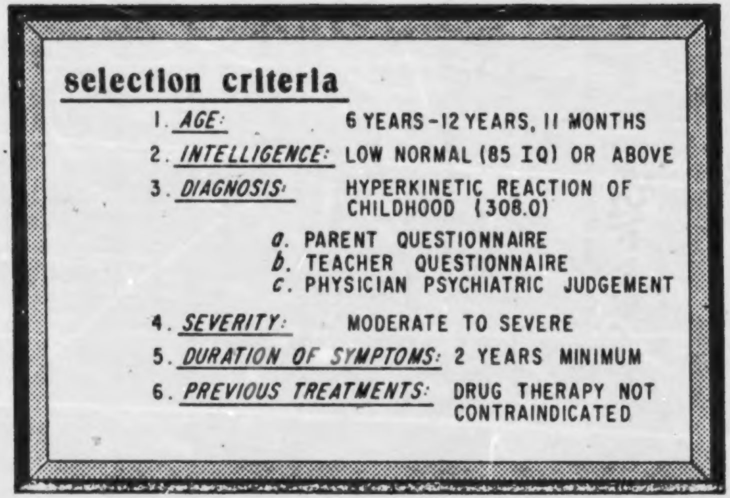
Table 2

Age Distribution of Sample

Age in Months*	%	N
61-84	6.7	1
85-108	53.3	8
109-132	33.3	5
133-156	6.7	1

*Mean Age = 105.4 months (8.78 years)

Table 3



selection criteria

1. *AGE:* 6 YEARS - 12 YEARS, 11 MONTHS

2. *INTELLIGENCE:* LOW NORMAL (85 IQ) OR ABOVE

3. *DIAGNOSIS:* HYPERKINETIC REACTION OF CHILDHOOD (308.0)

- a. PARENT QUESTIONNAIRE
- b. TEACHER QUESTIONNAIRE
- c. PHYSICIAN PSYCHIATRIC JUDGEMENT

4. *SEVERITY:* MODERATE TO SEVERE

5. *DURATION OF SYMPTOMS:* 2 YEARS MINIMUM

6. *PREVIOUS TREATMENTS:* DRUG THERAPY NOT CONTRAINDICATED

Design. Prior to treatment parents and teachers independently completed bi-weekly questionnaires regarding the child's current behavior, utilizing the abbreviated 10-item symptom scale ("pre-treatment period"). These measures were collected for two weeks, and then if the child was on medication, the medication was discontinued and the ratings continued for another two weeks ("baseline period"). If the child was not on medication, the ratings were similarly collected for the two-week baseline period.

At this point the children were randomly assigned to either the experimental (KP) diet, or a control diet. Parents and teachers continued to observe the children with weekly symptom ratings for four weeks. At this point the parents were interviewed by the principal investigator, the school reports were examined, and a judgment was made without knowledge of the diet condition as to overall global improvement, using the Clinical Global Impressions (CGI) scale. The same procedure was then followed for the next one month while the child was on the alternative diet. A summary of the experimental procedure appears in Table 4, and Table 5 lists the instruments used to document the trial.

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Tables 4 and 5 here

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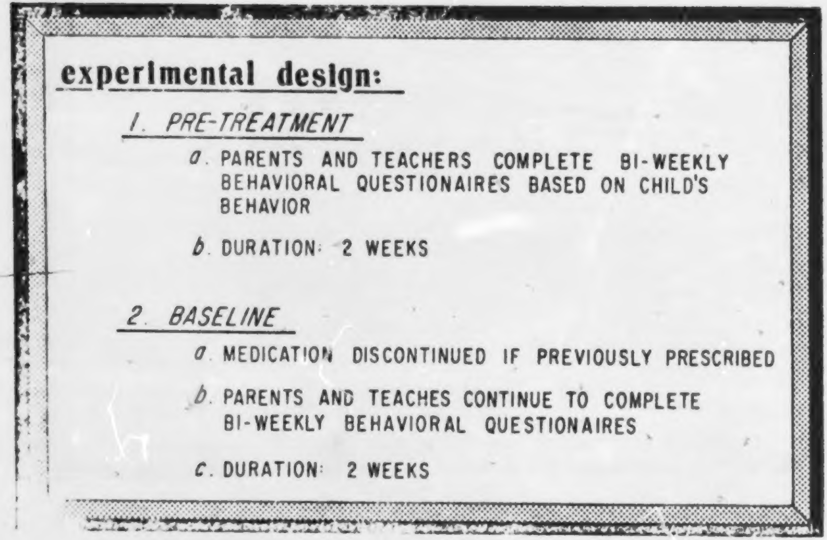
Appendix I contains the various forms used for data collection.

Table 4



experimental design:

1. PRE-TREATMENT

a. PARENTS AND TEACHERS COMPLETE BI-WEEKLY BEHAVIORAL QUESTIONAIRES BASED ON CHILD'S BEHAVIOR

b. DURATION: 2 WEEKS

2. BASELINE

a. MEDICATION DISCONTINUED IF PREVIOUSLY PRESCRIBED

b. PARENTS AND TEACHES CONTINUE TO COMPLETE BI-WEEKLY BEHAVIORAL QUESTIONAIRES

c. DURATION: 2 WEEKS

experimental design: *(cont.)*

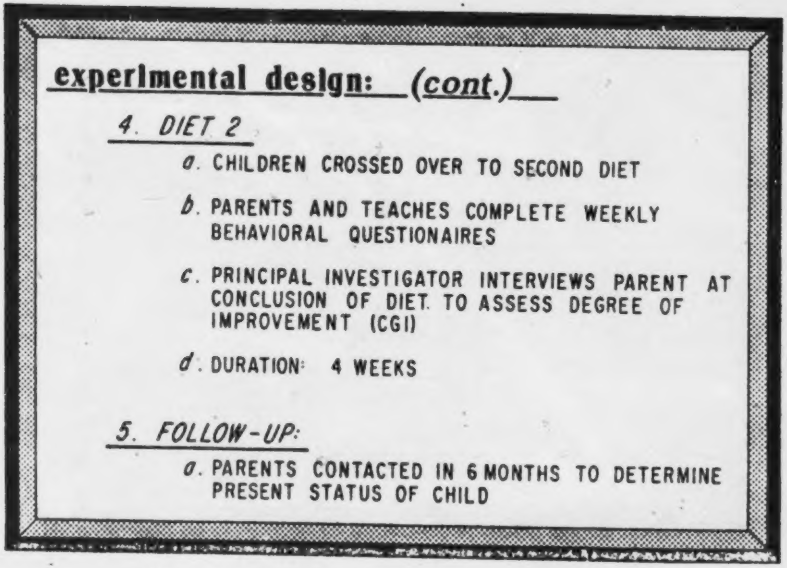
3. DIET I

a. CHILD RANDOMLY ASSIGNED TO EITHER EXPERIMENTAL OR CONTROL DIET

b. PARENTS AND TEACHERS COMPLETE WEEKLY BEHAVORIAL QUESTIONAIRES

c. PRINCIPAL INVESTIGATOR INTERVIEWS PARENTS AT CONCLUSION OF DIET TO ASSESS DEGREE OF IMPROVEMENT (CGI)

d. DURATION: 4 WEEKS



experimental design: (cont.)

4. DIET 2

- a. CHILDREN CROSSED OVER TO SECOND DIET
- b. PARENTS AND TEACHES COMPLETE WEEKLY BEHAVIORAL QUESTIONAIRES
- c. PRINCIPAL INVESTIGATOR INTERVIEWS PARENT AT CONCLUSION OF DIET TO ASSESS DEGREE OF IMPROVEMENT (CGI)
- d. DURATION: 4 WEEKS

5. FOLLOW-UP:

- a. PARENTS CONTACTED IN 6 MONTHS TO DETERMINE PRESENT STATUS OF CHILD

Table 5

measurement instruments:

1. CONNERS TEACHER QUESTIONNAIRE
2. CONNERS PARENT QUESTIONNAIRE
3. CONNERS PARENT-TEACHER QUESTIONNAIRE
4. PHYSICAL AND NEUROLOGICAL EXAMINATION FOR SOFT SIGNS
5. CHILDREN'S PSYCHIATRIC RATING SCALE
6. CLINICAL GLOBAL IMPRESSIONS
7. CHILDREN'S DIAGNOSTIC SCALE
8. CHILDREN'S DIAGNOSTIC CLASSIFICATION
9. CHILDREN'S PERSONAL DATA INVENTORY

Experimental and control diets. Prior to the start of the diets the parents met with the nutritionist (D.A.S.) who explained the particular diet the child was assigned to, giving the parent a list of items to be excluded, as well as a list of acceptable items. Procedures regarding compliance were discussed and general matters regarding food selection, preparation and recording were outlined.

The control diet was devised with the following criteria in mind: (1) The diet should involve the same degree of time in preparation, shopping and monitoring as the K-P diet; (2) the items in the control diet should be drawn from the same food groupings and categories where possible as the K-P diet; (3) the two diets should be nonoverlapping; i.e. items on the control diet should allow for eating of items excluded on the K-P diet, and vice versa; (4) the control diet should be as palatable and easy to follow as the K-P diet; (5) the control diet should appear plausible and reasonable as a possibly effective treatment.

With regard to this last point, care was taken in the instructions to parents to make each diet seem worthwhile and as likely to provide benefit as the experimental diet. At no times were the words K-P, Feingold diet, experimental diet, or control diet used. Instead, parents were told that their child would try both diets, that either might produce improvement, and that it was necessary to have both diets to compare with each other. They were told we were studying dietary factors in behavior problems, and that there might be a number of separate food items that could cause behavioral difficulties, and that only by systematically comparing different approaches could we be sure which diet(s) might be effective for their child. The two exclusion diets and suggested items available on each diet are provided in Appendix II.

Assessment of Prior Dietary Status. A nutritionist collected dietary information on each child using a dietary questionnaire, 24-hour recall, and food frequency measure.

Dietary Questionnaire - Parents supplied information pertaining to the food habits of their child -- number of meals and snacks per day, foods eaten for meals and snacks, meal times, food likes and dislikes, problems at the meal table, food allergies and other medical complications (See Appendix II).

24-hour Recall - Parents were asked to recall everything consumed by the child during the previous day. The time, place, a description of preparation and judged amount for each food item were also recorded. Food models were used to assist in assessing the amount.

Food Frequency Measure - Given a list of foods, parents were asked to indicate the number of times or frequency each food is usually consumed by their child during a "typical" week (See Appendix II).

The twenty-four hour recall, frequency and questionnaire were used together to determine the adequacy of prior dietary habits of the children (Adelson, 1960; Beal, 1967; Burke, 1947; Stefanik, et. al., 1962; Chalmers, et. al., 1952). Data from recall and frequency were grouped according to the basic four food groups, and with the data from the questionnaire, judged for adequacy and appropriate dietary patterns which would be conducive to sound nutritional practices. Problems or poor eating habits were discussed with the parents.

Dietary Compliance and Nutrient Monitoring. During the 12 week program, parents kept diet records, recording everything their child consumed, for 6 days each month. The time, place, food, a detailed description and the method of preparation, and the weighed or measured amount consumed were to be recorded. Three to seven day diet records have been shown to give reliable dietary information for nutrient analysis (Beal, 1967; Chalmers, et. al., 1952). In addition, parents maintained a list of infractions that occurred during each of the diet periods, and completed a dietary degree of difficulty questionnaire at the conclusion of each diet period to assess the comparability of the difficulty in following the control and experimental diets (see Appendix II).

Determination of Nutrient Intake. Diet records were coded using the USDA Home & Garden Handbook, No. 72, Nutrient Value of Foods, and analyzed with the Diet Research Program for calories, protein, carbohydrate, fat, calcium, iron, Vitamin A, thiamin, riboflavin, niacin, and Vitamin C. Averages for the nutrients were calculated for each individual based on the 6 day diet record (representing one month) for the three month periods, i.e., 3 sets of averages for each individual. Group averages were tabulated for each month period.

The computed nutrient intake data reported the contribution in gram units and percent made by meals (breakfast, lunch, dinner and snack) for individuals and group. Percentages of the Recommended Dietary Allowances were calculated for breakfast, lunch, dinner and snack; total for each individual average intake; and for the group intake during baseline, K-P diet and control diet.

Recommended Dietary Allowances. The Recommended Dietary Allowances (RDA) are the levels of intake of essential nutrients considered, in the judgement of the Food and Nutrition Board on the basis of available scientific knowledge, to be adequate to meet the known nutritional needs of practically all healthy persons.

In order to meet these needs, the levels of nutrients listed in the RDA have an added margin of safety to cover individual variation. The RDA was established as a standard for populations. When dealing with individuals or small groups, 2/3 of the RDA is, by convention, taken as a cut-off point in assessing adequate or poor diets.

Levels of nutrients listed by the RDA have been categorized by sex and age groupings. Thus, the percentages of the RDA tabulated from the dietary records in the present study have incorporated both sex and age of the subjects studied.

Appendix III contains a detailed flow sheet of the different types of contact with the parents, teachers, and patients.

Results

Clinical Global Impressions. Table 6 shows the principal investigator's judgement of improvement based upon interview with the parents, the parent symptom ratings, and the teachers' symptom ratings. The project coordinator (C.H.G.) met with parents prior to each of the two final interviews following each diet, and reminded parents not to mention any specific foods involved in the diet. The Principal Investigator (C.K.C.) also reminded the parents at the start of the interview not to reveal which diet their child had been on. Then a semi-structured interview was conducted in which the parents' view of overall changes, somatic changes, peer and family changes, the child's reaction to the diets and any knowledge of changes in school were elicited. At this point, if the interview was following the first diet, regardless of what changes the parent noted or failed to find, the parent was strongly exhorted to give the other diet a fair try, to be scrupulous in following and monitoring it, and to encourage the child to follow the new diet. If the child had improved, parents were told he conceivably could improve even more on the second diet, and if unimproved, the second diet might offer hope of more change. In this way an effort was made to have the second diet uninfluenced by results from the first diet.

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Table 6 here

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Table 6 shows that significantly more of the K-P diet trials were rated as improved than the control diet, using a Wilcoxon signed ranks test ($p < .01$).

Teacher and parent ratings. Table 7 presents the summary of hyperkinesis index scores for the two raters, together with

Table 6

Clinical Global Impressions

		Feingold Diet				
		0	+1	+2	+3	
Control Diet	0	4	4	3	0	11
	+1	1	1	0	1	3
	+2	0	0	1	0	1
	+3	0	0	0	0	0
		5	5	4	1	15

Note: 0 = Unchanged or Worse
+1 = Minimal Improvement
+2 = Moderate Improvement
+3 = Marked Improvement

Wilcoxon Matched-Pairs Signed-Ranks Test:

$p = 0.01$ (one-tailed)

a summary of statistical analyses. Table 8 presents hyperkinesis index scores broken down by the order in which each treatment was received. The data indicate that the K-P diet is significantly more effective than the control diet for the teachers ($p < .005$), but not for the parents, while for both teachers and parents the K-P diet is significantly better than the baseline period, ($p < .05$), whereas the control diet does not differ from the baseline.

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Tables 7 and 8 here

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Figure 1 shows that both parents and teachers note approximately a 15% reduction in symptoms on the K-P diet, relative to a 3% or smaller reduction on the control diet. Figure 2 shows the same data broken down by order of treatment, where it may be seen that the bulk of the improvement on the K-P diet was noted when it followed the control diet (although the order effect was not quite significant ($p = .07$).

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Figures 1 and 2 here

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Figures 3 and 4 show the average hyperkinesis index scores for all patients across the 12 weeks of the study, for parents and teachers, respectively. Figures 5 and 6 present data from

PARENT AND TEACHER RATINGS OF HYPERKINETIC BEHAVIOR ACROSS TREATMENT

Table 7

MEAN HYPERKINESIS INDEX SCORES

TREATMENT	RATERS	
	PARENTS	TEACHERS
BASELINE	16.30	16.48
CONTROL DIET	15.72	17.18
K-P DIET	13.77	13.93

LEVEL OF SIGNIFICANCE BETWEEN TREATMENTS (ANALYSIS OF VARIANCE)

DIET COMPARISON	PARENTS	TEACHERS
K-P vs BASELINE *	<0.05	<0.05
CONTROL vs BASELINE	NS	NS
K-P vs CONTROL *	NS	<0.005

NS = NOT SIGNIFICANT AT THE 0.05 LEVEL

* ALL DIFFERENCES IN FAVOR OF K-P DIET

Table 8

Rater	Pre-treatment	K-P Diet	Control Diet
Parent reports			
K-P 1st (N=9)	16.83	16.11	16.28
Control 1st (N=6)	15.50	10.25	14.87
Combined	16.30	13.77	15.72
Teacher reports			
K-P 1st (N=9)	16.22	15.53	18.22
Control 1st (N=6)	16.88	11.54	15.63
Combined	16.48	13.93	17.18

Figure 1

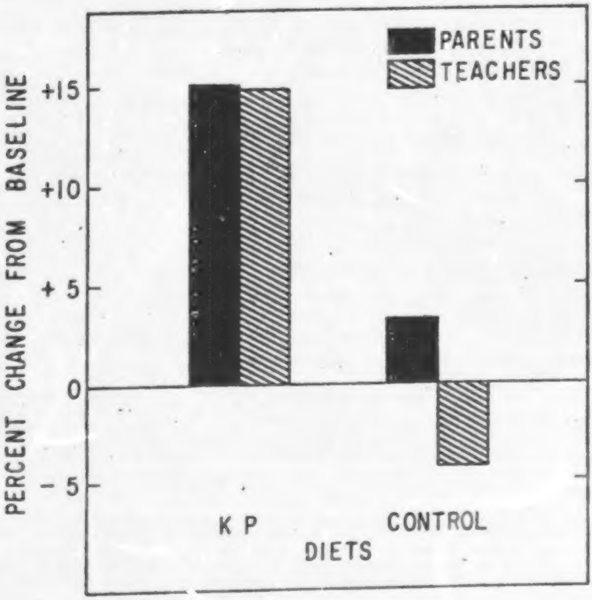
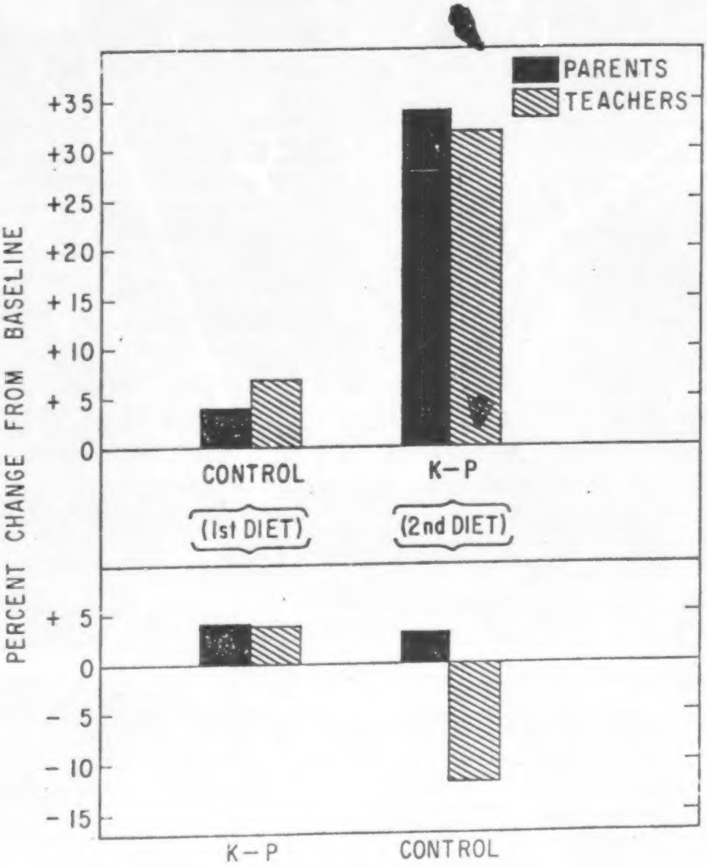

PARENTS
TEACHERS
PERCENT CHANGE FROM BASELINE
+15
+10
+ 5
0
- 5
K P
CONTROL
DIETS

Figure 2


PARENTS
TEACHERS
PERCENT CHANGE FROM BASELINE
+35
+30
+25
+20
+15
+10
+5
0
CONTROL
(1st DIET)
K-P
(2nd DIET)
+5
0
-5
-10
-15
K-P
CONTROL

two individual subjects which illustrats the remarkably close agreement between changes in behavior noted by parents and teachers at different points in the experiment. The congruence of these ratings provides assurance that the fluctuations are probably reflecting real behavioral changes and not idiosyncratic rating errors or unreliability of the scales.

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Figures 3 - 6 here
- - - - - - - - - - -

Tables 9 and 10 show the analyses of variance for the teacher data for raw scores and baseline-corrected (difference) scores. In the latter procedure, the mean of the baseline scores was subtracted from the mean of the scores for each diet period to correct for initial starting level of symptoms prior to treatment. Similar analyses for the parent data are presented in Tables 11 and 12.

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Tables 9 - 12 here
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The raw scores for each of the periods of the study, for the different treatments and treatment orders for parents and teachers are presented in Appendix IV. Appendix V presents the informal comments of teachers as these were noted on the symptom questionnaires filled out at the end of the two diet periods.

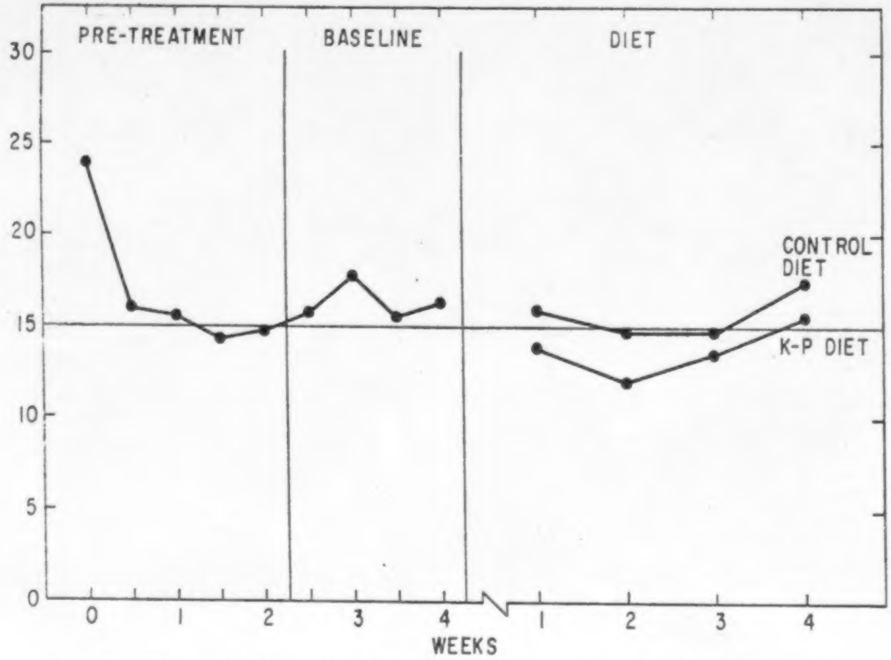


Figure 3

PARENT SYMPTOM REPORT FOR 15 PATIENTS AT PRE-TREATMENT, BASELINE (OFF MEDICATION) AND CONTROL OR KP DIET (EACH S HAD BOTH DIETS ASIGNED IN RANDOM ORDER)

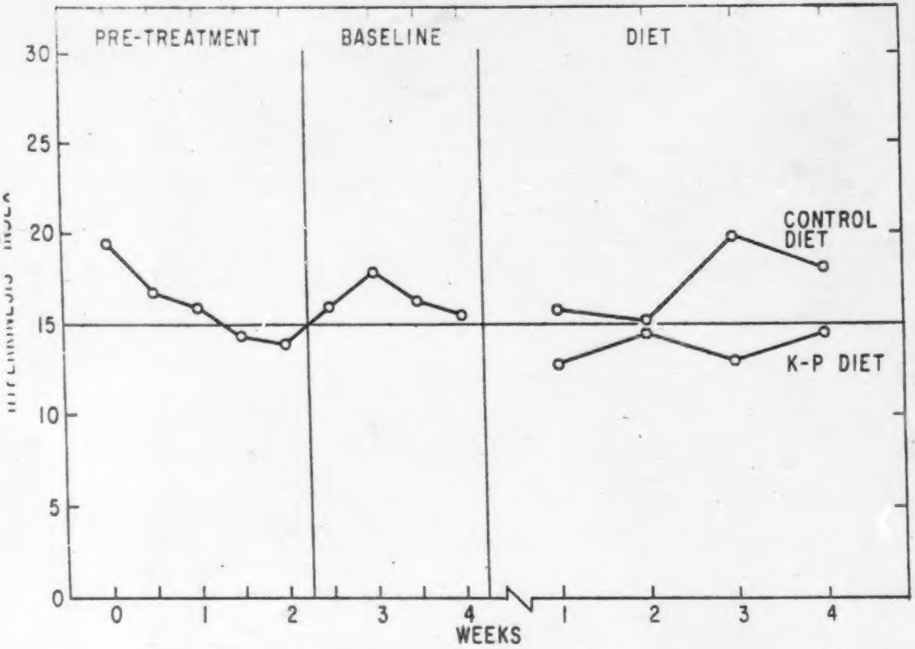


Figure 4

SCHOOL TEACHER SYMPTOM REPORT AT BASELINE AND ON EACH DIET

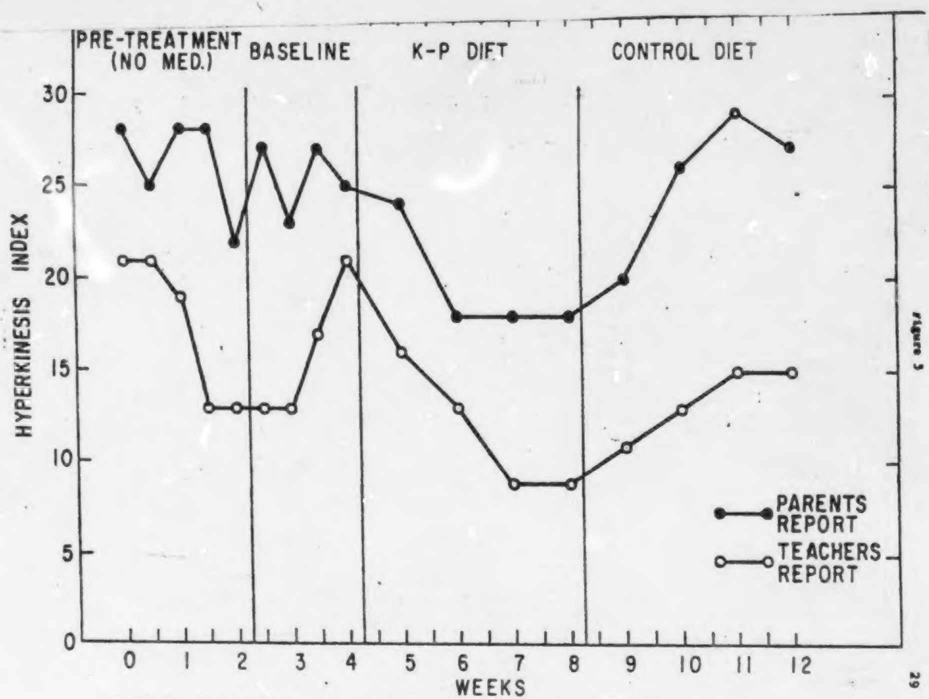
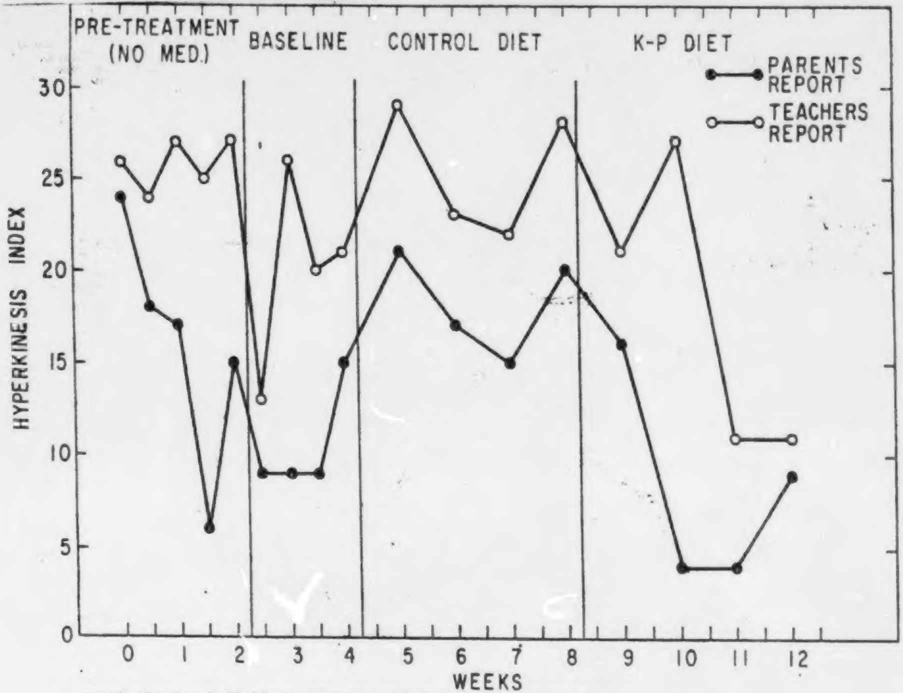


Figure 3

Graph showing individual case over 12 week treatment period. Lower score indicates improvement on hyperkinesis index



Graph showing individual case over 12 week treatment period

Figure 6

Table 9

ANALYSIS OF VARIANCE: BASELINE VS KP DIET TEACHERS

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW, SUBJ	1444,604	14			
GROUPS	20,000	1	20,000	0,183	0,6786
ERROR	1424,604	13	109,585		
WITHIN SUBJ	228,539	15			
BASELINE-KP	65,401	1	65,401	6,834	0,0204
GP X BASELINE-KP	38,735	1	38,735	4,048	0,0629
ERROR	124,403	13	9,569		
TOTAL	1656,510	29			

Table 10

```
ANAYLSIS OF VARIANCE:  KP DIET VS CONTROL DIET        TEACHERS    CURRECTED

SOURCE OF            SUMS OF     DEGREES OF     MEAN
VARIANCE             SQUARES      FREEDOM      SQUARE       F         P

BETW. SUBJ           533,363         14

 GROUPS              112,022          1        112,022    3,456    0,0830
 ERROR               421,340         13         32,411

WITHIN SUBJ          166,001         15

 KP-CONTROL           82,689          1         82,689   13,464    0,0031
 GP X KP-CONTROL       3,472          1          3,472    0,565    0,5286
 ERROR                79,840         13          6,142

TOTAL                695,894         29
```

Table 11

ANALYSIS OF VARIANCE: BASELINE VS KP DIET PARENTS

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	494,779	14			
GROUPS	93,168	1	93,168	3,016	0,1031
ERROR	401,611	13	30,893		
WITHIN SUBJ	276,880	15			
BASELINE-KP	64,201	1	64,201	4,748	0,0462
GP X BASELINE-KP	36,901	1	36,901	2,729	0,1195
ERROR	175,778	13	13,521		
TOTAL	755,592	29			

Table 12

ANAYLSIS OF VARIANCE: KP DIET VS CONTROL DIET PARENTS CORRECTED

SOURCE OF VARIANCE	SUMS OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	P
BETW. SUBJ	522,242	14			
GROUPS	38,042	1	38,042	1,021	0,3322
ERROR	484,200	13	37,246		
WITHIN SUBJ	281,153	15			
KP-CONTROL	41,328	1	41,328	2,633	0,1257
GP X KP-CONTROL	35,778	1	35,778	2,279	0,1522
ERROR	204,047	13	15,696		
TOTAL	790,585	29			

Prior Dietary Habits. Inspection of the 24-hour recall, dietary questionnaire, and food frequency measure indicated profound individual differences in the 15 children participating in the study. Two children had dietary habits which could be considered poor in most respects and which would likely worsen on restrictive diets without close supervision: one child had a good appetite, but did not like and rarely ate fruits and vegetables -- this child's diet consisted mainly of cereal with milk, crackers and cheese, and bread; the second child was reported to have a poor appetite and be a picky eater who would not eat anything he did not like, particularly vegetables -- he would not eat anything if one of his food dislikes was among the foods served.

Six children had some dietary habits which, though presently not a problem, could develop in the future into various forms of malnutrition. Two of these six children were reported by the mother to be overweight, and four were "picky" eaters and usually avoided foods they did not like - notably fruits and vegetables.

The remaining seven children were reported to be good eaters with no apparent nutritional problems.

Nutrient Analyses of Diet Records.

Pretreatment-Baseline - Nutrient analysis from diet records kept during pretreatment-baseline seemed to indicate that the nutrient intake for the group was good to adequate. Table 13 reveals the percentage of the RDA of calories and 8 nutrients for the group's average period intake. During this period, all nutrients exceeded 66% of the RDA with protein, calcium, Vitamin A, riboflavin, and Vitamin C exceeding 100% of the RDA. However, large individual variation existed as can be seen from the magnitude of the standard deviations also presented in this table. Thus although there were no apparent nutrient deficiencies in the nutrients analyzed, the possibility that certain individuals may have undesirable intakes does exist (Note: the nature of the RDA is such that evaluation of individuals should not be made on analysis of intake alone [e.g., individual needs vary and may not compare similarly to a standard]; for this reason individual comparisons will not be discussed further).

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Table 13 here

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Adequacy of Intake on Trial Diets - Nutrient intake during M-P and control diet periods are also presented in Table 13. As was the case with the pretreatment-baseline

Table 13

Percentage RDA and Standard Deviation of Group's Intake during Pretreatment-Baseline, Control and K-P Diets

	Pretreatment-Baseline		Control		K-P	
	%RDA	s.d.	%RDA	s.d.	%RDA	s.d.
Calories	80.4	24.8	82.1	29.1	76.6	30.4
Protein	204.7	62.3	206.3	64.2	194.3	58.5
Fat (gm)	(79.5)	(27.4)	(75.5)	(33.7)	(77.6)	(33.5)
CHO (gm)	(228.5)	(68.9)	(242.6)	(71.5)	(215.3)	(80.5)
Calcium	127.9	59.1	120.9	60.7	105.7	46.9
Iron	99.3	35.5	99.6	36.6	92.9	28.6
Vitamin A	128.5	137.7	123.7	85.7	107.3	122.8
Thiamin	95.8	43.5	91.9	47.6	83.4	36.4
Riboflavin	157.5	65.0	151.1	67.8	133.8	48.8
Niacin	84.2	38.6	78.3	35.7	94.3	48.2
Vitamin C	221.2	182.4	239.5	204.9	140.9	110.4

period, the nutritional intake during both trial diets was good to adequate, with all nutrients exceeding 66% of the RDA.

Treatment Differences - Statistical analyses comparing nutritional intake while following the K-P diet vs. pretreatment-baseline indicated lower calcium, riboflavin and Vitamin C on the K-P diet (similar trends were observed with all other nutrients with the exception of niacin). Comparisons between K-P and control diets revealed only two statistically significant differences: carbohydrate intake was less on the K-P diet, but niacin intake was greater. No differences were observed between the control diet and pretreatment-baseline.

Contribution of Breakfast - Reports have been made that the consumption of breakfast has a direct bearing on a person's activities during the morning. It is generally suggested that breakfast supply 1/3 of the days calories and nutrients. Table 14 shows the percent contribution made by selected nutrients to breakfast during the three periods. For this group, most nutrients are considerably less than 33%. Apparently breakfast was a small meal consisting of dairy food, grain food and a source of Vitamin C. The K-P diet severely reduced the Vitamin C sources taken at breakfast.

- - - - - - - - - -

Table 14 here

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Table 14

Percentage Contribution made by Breakfast to Group's Average Daily Intake during Pretreatment-Baseline Control and K-P Periods

	Pretreatment-Baseline	Control	K-P
Calories	17	16	15
Protein	15	14	14
Calcium	22	20	23
Iron	17	18	15
Vitamin A	14	15	11
Thiamin	22	26	20
Riboflavin	20	21	21
Niacin	11	15	10
Vitamin C	30	31	18

Dietary Degree of Difficulty and Dietary Compliance Measures. The dietary degree of difficulty questionnaires were converted to numerical scores (See Appendix) and averaged for each diet (possible score of 0 to 25, 25 being very difficult to follow). The mean dietary degree of difficulty score, as reported by parents, was 8.27 for the control diet and 9.53 for the K-P diet, indicating that the K-P diet perceived to be slightly more difficult to follow than the control diet.

The mean number of infractions reported per week for each of the diet periods was 1.50 for the control diet and 1.33 for the K-P diet, indicating close adherence to both diets. Viewed in conjunction with the dietary degree of difficulty questionnaire results, these data indicate a high degree of correspondence between diets on measures of overall dietary difficulty.

Discussion

The results of this study strongly suggest that a diet free of most natural salicylates, artificial flavors and artificial colors reduces the perceived hyperactivity of some children suffering from hyperkinetic impulse disorder. Teachers who observed the children over a 12-week period without knowledge of when the child started his diet and without knowledge of the fact that there were two diets which were employed, rated the children as less hyperactive while the children were on the diet recommended by Feingold. The difference obtained between the ratings when the children were on the K-P diet and when they were on the control diet would have occurred by chance only 5 times in one thousand. Similarly, the teachers rated the children as significantly improved over the baseline period at the beginning of the study while on the K-P diet but not while on the control diet.

The results from ratings by parents are slightly different in that parents do not detect a difference in behavior between the K-P and control diets, although they note the effect as compared with the baseline period. The fact that the parents do not detect a difference between the two special diets could mean that subjective factors associated with a change in diet of any kind mask whatever therapeutic effect might be present in the K-P diet. This interpretation is supported by the fact that whereas the baseline means for parents and teachers are very similar (16.3 and 16.5, respectively), the control diet means are somewhat different (15.7 vs. 17.2).

Another possibility is that the children are in fact not noticeably different at home, but are observed to respond better in a more structured situation where task expectations are clearly established, and where the teacher has a long baseline of comparison of the same children over many months. Similar findings of weak or marginal effects on behavior as rated by parents in contrast to clear effects noted by teachers has been found in drug studies with hyperkinetic children. It has been generally assumed that the demands on the child's attention and goal-oriented behavior are greater in the classroom and therefore that any improvements in these areas will be more evident.

It was found in this study that the bulk of the positive changes noted by both parents and teachers occurred in the group that started with the control diet and then switched to the experimental diet. Such an effect could be due either to the fact that the more responsive children happened, by chance, to fall into the sequence involving the control diet first; or the results could be due to the fact that the observers have a clearer basis on which to judge improvement after the control diet has failed to produce any noticeable changes. Although this finding weakens the argument that the obtained differences are reflecting the K-P diet rather than some nonspecific factors, it should be noted that such findings are quite common in psychopharmacologic research involving crossover designs. For example, in a double-blind crossover study involving dextroamphetamine and hyperkinetics, (Conners, Eisenberg and Barcai, 1967), the following results were obtained on the teacher questionnaire (using a somewhat different set of items):

	Pre-Treatment	Dexedrine	Placebo
Drug 1st (N=28)	29.1	20.6	26.00
Placebo 1st (N=24)	22.6	12.8	21.2
Combined	25.6	16.7	23.6

It is clear that the drug effect is much more pronounced in the group which received placebo first. Thus, even when objective measures substantiate improvement in behavioral functioning in the first period of evaluation, the teachers may be less aware of the improvement until they see the lack of improvement on another treatment.

Inspection of the individual ratings of children in the study shows that only four or five of the children were seen as improved by both parents and teachers. This fact is apparent from inspection of the clinical global impressions which took into account both parent and teacher effects. The findings suggest that there may be a small subgroup of hyperkinetic children who are showing the changes induced by the K-P diet. Further research will be required to determine if such children are physiologically different from non-improvers. Another possibility needing further evaluation is that somehow the blind of the experiment, the bias of the parents, or communication between parent and teacher regarding the diets served to bias the results in the children rated as improving. It seems unlikely on the face of it that teachers would detect a significant effect when they are unaware that two diets are involved. On the other hand, if enthusiastic parents communicated to teachers when the diets were changed, the obtained results would be entirely spurious.

It is important to note that dietary compliance and degree of difficulty following the diets were comparable for the control and K-P diets. The K-P diet may have been slightly more difficult to follow, but there were also slightly fewer infractions, suggesting that the effects are unlikely to reflect any real difference in the difficulty of maintaining the child on the diets.

It would be hazardous at this point to draw too many conclusions from this experiment, given the small size of the sample and the lack of complete consistency in the results. Any thoughtful observer will understand that a major intervention into dietary habits of a family will produce behavioral effects, regardless of the specific diets, a phenomenon well understood in the management of such conditions as juvenile diabetes. The results would have been substantially clarified if it had been possible to have objective measures of function uncontaminated by the psychological factors which are bound to operate in the family-school-child system. At this point the results point to the need for considerable further investigation.

One of the difficulties in testing the Feingold hypothesis is that the independent variable--the foods being varied in the experiment--is so nonspecific. We cannot say whether the natural salicylates, food colors, food flavors--or indeed unsuspected nutritional factors--might not be responsible for the results. For example, we found that, among other things, carbohydrate intake was significantly less on the K-P diet. In view of a commonly held argument that many hyperkinetics suffer from hypoglycemia, it is conceivable that such an unintended effect of the diet is producing the improvement seen by parents and teachers.

A matter of some concern is the extent to which the K-P diet reduced the nutrient intake of the children. As a group the children still had intakes above the recommended daily allowances, but dietary problems could arise for certain individuals over a prolonged period of time. Dietary counseling and/or careful monitoring by a physician should be considered until the long-term effects of the diet can be evaluated more thoroughly. It was particularly notable that the children as a whole were poor in terms of the contribution of breakfast to the total recommended daily allowance of nutrient intake, and the fact that vitamin C is substantially reduced on the K-P diet makes the role of breakfast potentially more of a problem in this group of children.

The higher values of Niacin on the K-P diet has no ready explanation. Considering the number of comparisons examined statistically, this may be a chance finding of dubious significance from a practical point of view.

Summary and Recommendations

A double-blind crossover trial involving a control diet and a diet eliminating artificial flavors, colors and natural salicylates as recommended by Feingold was conducted on 15 hyperkinetic children. Teachers and parents observed the children for one month prior to treatment, using standardized rating scales. Both parents and teachers reported fewer hyperkinetic symptoms on the K-P diet as compared to the pre-treatment baseline ($p < .05$). The teachers noted a highly significant reduction of symptoms on the K-P diet as compared to the control diet ($p < .005$) but the parents did not. The control diet ratings did not differ from the baseline period ratings for either parents or teachers.

It is concluded that the K-P diet may reduce hyperkinetic symptoms, though this result is put forth with caution in view of several features inherent in the present study which need further evaluation, including objective measures of change, manipulation of the independent variable and reducing the independent variable to more specific components.

The K-P diet produced consistently poorer nutrient intake than the control diet or baseline period, especially for vitamin C. However, the effects were not nutritionally serious inasmuch as the children were still having nutrient intake above the recommended daily allowances. Long-term consequences of the diet would have to be followed with caution.

The following recommendations are made:

(1) Further studies employing objective measures, challenge testing of the putative harmful agents, and other controls are required before definitive recommendations are made on any large scale basis;

(2) Careful monitoring of nutritional status and dietary habits are recommended before children are placed on the K-P diet.

(3) Food intake at breakfast needs especial care in hyperkinetic children;

(4) Biochemical and clinical testing to determine the possible mechanisms involved should be undertaken, especially on clearly defined subjects who improve on the K-P diet, but further validation of the basic clinical effects is still required.

References

Adelson, S.F. Some problems in collecting dietary data from individuals. J. Amer. Diet. Assoc., 1960, 36, 453.

Beal, V. The nutritional history in longitudinal research. J. Amer. Diet. Assoc., 1967, 51, 426.

Burke, B. Dietary history as a tool in research. J. Amer. Diet. Assoc., 1947, 23, 1042.

Chafee, F. H. and Settipane, G. A. Asthma caused by FD&C approved dyes. J. Allergy, 1967, 40(2), 65-72.

Chalmers, F. W., et. al. The dietary record - how many and which days. J. Amer. Diet. Assoc., 1952, 28, 711.

Conners, C. K. A teacher rating scale for use in drug studies with children. Amer. J. Psychiat., 1969, 126(6), 884-888.

Conners, C. K. Symptom patterns in hyperkinetic, neurotic and normal children. Child Devel., 1970, 41, 667-682.

Conners, C. K., Eisenberg, L. and Barcai, A. Effect of dextroamphetamine on Children. Arch. Gen. Psychiat., 1967, 17, 478-485.

Feingold, B. B. Introduction to Clinical Allergy. C. C. Thomas, Springfield, Ill., 1973.

Food and Nutrition Board, National Research Council. Recommended Dietary Allowances. National Acad. Sciences, Washington, D.C., 1974.

Juhlin, L., et. al. Urticaria and asthma induced by food-and-drug additives in patients with aspirin hypersensitivity. J. Allergy Clin. Immun., 1972, 50, 92-98.

National Advisory Committee on Hyperkinesis and Food Additives. Report to the Nutrition Foundation. The Nutrition Foundation, Inc., 1975.

Sprague, R. L., Christensen, D. E. and Werry, J. S. Experimental psychology and stimulant drugs. In C. K. Conners (Ed.), Clinical use of stimulant drugs in children. Amsterdam: Excerpta Medica, 1974.

Stefanik, P., et. al. Determining the frequency intakes of foods in large group studies. Amer. J. Clin. Nutrit., 1962, 11, 335.

USDA Home and Garden Handbook #72. Nutritive Value of Foods. Superintendent of Documents, Washington, D.C., 1972.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
NATIONAL INSTITUTE OF EDUCATION
WASHINGTON, D.C. 20208

OFFICE OF THE DIRECTOR

11 SEP 1975

Honorable Edward M. Kennedy
Chairman, Subcommittee on Health
Committee on Labor and Public Welfare
U.S. Senate
Washington, D.C. 20510

Dear Senator Kennedy:

With your permission, I would like to submit a brief statement for the record of your September 11, 1975, hearings on "A New Method of Treating Hyperactive Children."

In 1973, NIE researchers interested in finding alternatives to drug treatment for hyperactive elementary school youngsters became aware of the work of Dr. Ben Feingold of the Kaiser Permanente Medical Center in San Francisco. Dr. Feingold's clinical experience with hyperactive children has led him to believe that food additives, especially artificial colors and flavors were an important contributing factor in this disorder and that dramatically favorable results could be achieved with some hyperactive youngsters by putting them on a diet free of these additives. NIE felt that there was enough plausibility to Dr. Feingold's hypothesis to warrant its being studied under controlled conditions.

In 1974, by competitive selection, NIE awarded a $60,000 contract for such a study to Dr. Keith Conners, currently Professor of Psychiatry at the University of Pittsburgh, and since the early 1960's a researcher eminent for his work in this field.

In this experiment Dr. Conners first determined the pre-diet levels of hyperactivity among 15 hyperactive children and then randomly assigned them to experimental and control groups. Those in the experimental group were placed on a diet free of artificial colors and flavors, those in the control group, on a diet containing the usual complement of food additives. The diets were comparable in terms of nutritional value and the degree of difficulty likely to be encountered in their implementation. The parents kept track of the food their children consumed and noted any dietary infractions.

Each week parents and teachers filled out a standard hyperactivity rating scale for the children in the experimental and control groups, and after one month Dr. Conners interviewed the parents and reviewed parent and teacher ratings in order to make a global judgment about each child's improvement, or lack of it. Parents were not told which diet was being tested, and neither the teachers nor Conners (at the time of the interviews) were told which diet any particular child was on.

At the end of the month the children on the experimental diet were placed on the control diet and vice-versa. Once again parents, teachers and Dr. Conners rated them on the hyperactivity scales.

Based on the teachers' ratings, traditionally the most reliable of the three, there was a statistically significant difference between the experimental and control treatments. Both parents' and teachers' ratings during the experimental diet indicated a significant improvement over the pre-diet period, whereas the control diet showed no such improvement. Further, according to Dr. Conner's global assessments, the children on the experimental diet did significantly better than those on the control diet. However, a comparison between parents' ratings for the experimental and control treatments showed no significant difference.

The study is now complete and Dr. Conners has concluded that the Feingold diet "may reduce hyperkinetic symptoms," though he urges caution in interpretation of the results and emphasizes the need for further research on the subject before any definitive recommendations are made.

Given the complexity of the issue and the ramifications of its resolution, NIE believes that the Conner's study is but a first step toward understanding the relationship between food additives and hyperkinesis. We also urge caution in its interpretation and use and recommend that further research be done in this area.

I am enclosing a copy of the Conners' report along with a detailed NIE staff analysis of its results. I will be most happy to answer any questions you might have about this study. Please let me know if you desire additional information.

Sincerely,

Harold L. Hodgkinson

Harold L. Hodgkinson
Director

Enclosure

NIE STAFF CRITIQUE OF CONNORS, ET AL., "FOOD ADDITIVES AND HYPERKINESIS: A CONTROLLED DOUBLE BLIND EXPERIMENT"

This is a pilot study and, as such, is a preliminary attempt to discover empirically whether, under certain specified conditions, there is statistical justification for the assertion that food additives, as characterized by Dr. Ben F. Feingold, are causally related to hyperkinesis in children.

Despite the title of the study, it is not, nor was it intended to be, a test of the effects of food additives per se. Rather it is a test of two diets -- the Feingold diet which contains no artificial colors or flavoring and the control diet which does in amounts commonly found in the marketplace.

As a test of two diets it is the investigators' conclusion that the results should be viewed with caution. As the investigators observe, the Feingold diet not only differs from the control diet with respect to certain food additives, but also with respect to the amount each diet contains of several common and essential nutrients, e.g., carbohydrates, vitamin C, niacin, thiamin and others. Thus, it is difficult to tell whether the behavior of the children on the Feingold diet changed because of food additives or because of nutritional differences. There is reason to believe such a distinction may be important. For example, the investigators call attention to the observed association of hyperkinesis and hypoglycemia, and indicate that hypoglycemia is dietarily regulated by, among other things, reducing carbohydrate intake. Since the Feingold diet has fewer carbohydrates than the control diet, the investigators note that part of the observed reduction in hyperkinesis attributed to reduced food additives could as well be attributed to the attenuated effects of hypoglycemia. The possibility of other uncontrolled effects due to dietary differences cannot be discounted.

Two other significant sources of uncertainty in the study are its small sample size (15 children), and the uncertain control of the information and expectations held by the parents. In the first instance a review of the literature and statistical considerations suggested that a sample size of 80 children would be large enough to permit reliable estimates of statistical differences. That a significant effect is shown with just 15 children does not take away from the desirability of a larger sample in order to ensure and expand the generalizability of the results to children of diverse social and demographic characteristics.

A larger sample might also shed light on the unexplained finding that the behavioral effects of the diets are evidently related to the order in which they are administered to the children (Figure 2, p. 25 of report). That is, when the Fiengold diet is given first, followed by the control diet, the difference in the children's behavior between the two diets is not significant, and there is only trivial amelioration of behavior due to the Feingold diet. But when the Feingold is administered after the control diet, there appears to be a significant different between the two diets, and a marked reduction of hyperkinetic symptoms of those children using the Feingold diet. The investigators indicate that "order effects" of this kind are not an uncommon finding in other drug-related "double blind" research. Nonetheless, one would expect that if the observed effects were entirely or even largely due to dietary differences, then there would be consistent effects regardless of the order of presentation of the diets.

That effects are not consistent opens the possibility of alternative and competing interpretations of the data. One such alternative is that the parents and/or teachers are influenced through their awareness of differences between the diets, or some other uncontrolled exposure to information, and subsequently bias their own ratings of the children's behavior or, possibly, directly influence the behavior of the children. The study does not permit confident selection among the alternatives and thus it simply shows that while this particular formulation of the Feingold diet may reduce hyperkinetic behavior, it is also possible that the observed reduction is an artifact of the parents and teachers' belief that it will.

In addition to the foregoing primary concerns, there are a number of secondary issues which also have been exposed by the study and which will need consideration before embarking on further research or establishing policy with regard to food additives. These issues are largely methodological or questions of study design which might exert influence on the findings and which must be better understood in the assessment of the validity of these and future results. The issues are as follows:

1. Why should the control diet produce an increase in hyperkinetic behaviors reported by teachers and not by parents?
2. What are the pharmacological and behavioral implications of using subjects, some of whom, as in the pilot study, were on medication prior to the experiment, and some of whom were not?

3. What effect would the variation in prior dietary habits of the children have on the findings? Is there reason to suspect long term carry-over effects of pre-treatment diets?
4. How many and what types of related factors must be taken into account in defining and studying hyperkinesis? There are presumed associations between hyperkinesis and such factors as age, residential location, hypoglycemia, etc., each of which will limit the determinacy of future results unless we have sufficient awareness of their incidence, etiology, and effect to permit appropriate assumptions and controls.
5. What is the reliability and validity of the 10-item hyperkinesis index used, given that it is a short version derived from a much longer scale?
6. Although the analysis of variance has an "order of diet" term in the model (mislabeled as "group" in the report), Figure 2 p. 25 illustrates that the order effect may be worth investigating further.
7. The report and this figure use "baseline-corrected scores", which are the differences between the ratings of the children before and after they were placed on the diets. There are disadvantages in using difference scores for such analyses (including variance, unclear interpretive meaning, etc.,). Are there other, more effective ways to correct for initial differences in behavior of the children?

CONCLUSION

The pilot study concludes that findings should be reviewed with caution and this seems to be a fair statement. The behavioral outcome measures are "soft" and the pharmacology uncertain. The experimental design is subject to certain problems as the authors point out. The sample size does not allow for much further analysis. The question is whether or not to correct the design for stronger inferences, get more data, and continue this research. This does not seem to be a question that can be answered by statistics or analysis. Rather it is a question which must be addressed within and between the many relevant subject-matter areas, whose members, armed with theory and method, can objectively continue the exploration of this complex phenomenon.

The NIE Experiment on Food Additives and Hyperactivity

Background and Summary

In 1973 NIE researchers interested in finding alternatives to drug treatment for hyperactive elementary school youngsters became aware of the work of Dr. Ben Feingold of the Kaiser-Permanente Medical Center in San Francisco. Dr. Feingold's clinical experience with hyperactive children had led him to believe that food additives, especially artificial colors and flavors, were an important contributing factor in the disorder and that dramatically favorable results could be achieved with some hyperactive youngsters by putting them on a diet free of these additives. Dr. Feingold's hypothesis was and is controversial, in part because the evidence he adduced to support it was based on clinical observations rather than systematic research.

After a visit with Dr. Feingold and conversations with other doctors who had tried the diet, it was concluded that there was enough plausibility to the hypothesis to warrent its being investigated systematically. In the spring of 1974, then, NIE requested proposals for a controlled experiment to test the hypothesis. A $60,000 contract for the study was awarded to Dr. Keith Conners, currently Professor of Psychiatry at the University of Pittsburgh and since the early 1960's a researcher eminent for his work in this field.

In this experiment Dr. Conners first determined the pre-diet levels of hyperactivity among 15 hyperactive children and then randomly assigned them to experimental and control groups. Those in the experimental group were placed on a diet free of artificial colors and flavors, those in the control group, on a diet containing the usual complement of food additives. The diets were comparable in terms of nutritional value and the degree of difficulty likely to be encountered in their implementation. The parents kept track of the food their children consumed and noted any dietary infractions.

Each week parents and teachers filled out a standard hyperactivity rating scale for the children in the experimental and control groups, and after one month Dr. Conners interviewed the parents and reviewed parent and teacher ratings in order to make a global judgment about each child's improvement, or lack of it. Parents were not told which diet was being tested, and neither the teachers not Conners (at the time of the interviews) were told which diet any particular child was on.

At the end of the month the children on the experimental diet were placed on the control diet and vice-versa. Once again parents, teachers and Dr. Conners rated them on the hyperactivity scales.

Based on the teachers' ratings, traditionally the most reliable of the three, there was a statistically significant difference between the experimental and control treatments. Both parents' and teachers' ratings during the experimental diet indicated a significant improvement over the pre-diet period, whereas the control diet showed no such improvement. Further, according to Dr. Conner's global assessments, the children on the experimental diet did significantly better than those on the control diet. However, a comparison between parents' ratings for the experimental and control treatments showed no significant difference.

Dr. Conners concludes that the Feingold diet "may reduce hyperkinetic symptoms," though he urges caution in interpretation of the results and emphasizes the need for further research on the subject before any definitive recommendations are made.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ROCKVILLE, MARYLAND 20852

SEP 03 1976

Honorable Edward M. Kennedy
Chairman, Subcommittee on Health
Committee on Labor and Public Welfare
United States Senate
Washington, D.C. 20510

Dear Senator Kennedy:

As requested by Mr. Walter Sheridan of your Subcommittee staff, we are enclosing copies of the Transcript of Proceedings for the Interagency Group on Hyperkinesis, the First Report of the Preliminary Findings and Recommendations of The Interagency Collaborative Group on Hyperkinesis, and the Connors Study. These are for inclusion in the printed record of the hearing on September 11, 1975, before your Subcommittee.

If I can be of any further assistance, please let me know.

Sincerely yours,

Robert C. Wetherell, Jr.

Robert C. Wetherell, Jr., Director
Office of Legislative Services

3 Enclosures

TRANSCRIPT OF PROCEEDINGS

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

INTERAGENCY GROUP ON HYPERKINESIS

Date: September 30, 1975

Place: Washington, D. C.

BOWERS REPORTING COMPANY
7309 Arlington Boulevard
Falls Church, Virginia 22042
Phone: 703-573-5900

PROCEEDINGS

Dr. Kolbye. Ladies and gentlemen, I would like to open the opening session of the meeting. My name is Albert Kolbye. I am the Associate Director for Sciences, Bureau of Foods, Food and Drug Administration, and the Acting Chairman of the Interagency Collaborative Group on Hyperkinesis.

This is our second meeting as an interagency panel. Our primary purpose is to review the completed research, the ongoing research, and proposed research, and make preliminary findings and recommendations to the Assistant Secretary for Health and Scientific Affairs, Dr. Ted Cooper.

We will be making a preliminary report which hopefully will be delivered to the Assistant Secretary by the end of October.

Our purpose here as a group is to pool our expertise and our viewpoints in terms of evaluating where we are and where we need to go, to clarify the role of dietary modification in the behavior of hyperkinetic children.

As you all know, Dr. Feingold has pioneered in the area of evaluating dietary changes in relation to hyperkinesis; as a working group we are here to evaluate the evidence and to see what additional steps need to be undertaken to clarify the behavior changes that occur and what the basis is of those changes, and what mechanisms need to be explored to elucidate this entire matter. The representatives for the interagency panel include the National Institute of Education and various Institutes from the National Institutes of Health. For example, National Institute of Mental Health, Child Health and Human Development, Neurological Diseases, and the rest of whatever that title is. I think it is communicative disorders and stroke. And of course a representation from the Food and Drug Administration in both the Bureau of Drugs and the Bureau of Foods.

We have a relatively busy schedule today. Our purpose is to invite various people who are active in the research in this area to present whatever findings or comments they wish to present to us to share information with us as to the nature of the phenomena involved and what, in their viewpoint, would be helpful approaches to elucidate the entire matter.

In a moment I will ask each member of the interagency panel to raise his or her hand and introduce himself or herself so that the rest of the group here can at least identify who is on the interagency panel.

I will ask, during the course of the proceedings today, that each individual, be they guests or observers or panelists, precede each and every remark that he or she makes with his or her name, because in a room such as this the acoustics are not that good, and it is impossible for the transcribing technician to identify each and every person.

So I will appreciate your cooperation in that matter.

Incidentally, I do apologize for the close quarters. We are trying to improve the ventilation here. Suffice it to say that there are not too many conference rooms available that are capable of handling a group this size, and we have sort of grown as a group as more and more people have become involved or interested.

So in short, I welcome all of you here. I thank you for coming, and at this point I would like to, starting with my left, go around this table and introduce the panel members.

[General introductions.]

Dr. Kolbye. Apparently we are having some difficulties with the acoustics due to the ventilation in terms of transcribing. I would ask that each individual, when he or she speaks, to speak loudly and clearly, and let us see if we can get this transcribed.

I would like to call upon Dr. Keith Conners as our first visiting scientist to make his presentation. I believe the easiest thing, Dr. Conners, if you could sit at the end there. Incidentally, I hope, or I would like to ask, would you like to give your presentation and then open it up to questions, or will you entertain questions or comments part way through?

Dr. Conners. I would like to have the questions as people raise them.

Dr. Kolbye. OK.

Dr. Conners. What I am going to report to you today is a study which has been summarized in a report to the National Institute of Education. Any of you who have not seen that study and wish to obtain copies I presume can do so from David Boesel, from the National Institute of Education, who is here in the room.

I will try to be very brief, and outline the study to you, and then discuss what

I think are some issues in further study with the clinical population we call hyperkinetic behavior syndrome.

If I can have the first slide, please.

As you can see, the selection criteria for our study are listed there. These are 6- to 12-year-old children, an IQ of at least 85, with a clinical diagnosis by a board-certified child psychiatrist as hyperkinetic reaction of childhood. That diagnosis is made after a standardized clinical interview, and clinical history, as well as specific cutoff scores on the parent and teacher questionnaires.

The parent questionnaire is a 93 item symptom list, and the teacher questionnaire is a 39 item symptom checklist.

The physician uses a psychiatric rating scale which is a modification of one developed by Grunner and Graham (?), which requires a half hour interview with specific items of behavior to be rated.

We require that the children have had a history of hyperkinetic behavior for at least 2 years, and whether they had or had not had drug therapy, we accepted them for the study.

In the pilot study in Boston we had approximately 30 children, of whom 8 were accepted into the study. That study began in May and finished at the end of June because of the school year.

Next slide, please.

The measuring instruments are largely those that have been developed by the psychopharmacology branch of NIMH for drug studies in children, and the three questionnaires which I have developed are among the major dependent variables used in the study.

The PANSS or physical and neurological examination for soft signs is an objectively-scored pediatric neurological exam, the purpose of which was, as far as the overall plan of the study, to help subdivide the children into subgroups based upon physical signs as well as history.

The other instruments I will not go into in any detail. These are all documentation forms prepared in a packet by the Biometrics Lab of George Washington University for the National Institute of Mental Health Psychopharm Branch.

Next slide, please.

This just shows one of the off-scan forms, the 10 item subscale which I will be referring to later. The 10 item scale consists of 10 symptoms that both the teacher and the parent rate on the child, and it is selected from the larger version of the instruments, and has been found to have a very high correlation with the hyperactivity factor from both the parent and the teacher scale. Since it is 10 items it is easy to use, and the correlation is high enough with the pure factored scales that it is a reasonable instrument to use.

It consists of items such as restless, overactive, excitable, impulsive, disturbs other children, fails to finish things he starts, fidgeting, et cetera. In other words, the cardinal behavioral traits of the syndrome.

Next slide, please.

The experimental design that we used was essentially a baseline followed by a double blind crossover. What we call pretreatment consists of 2 weeks during which nothing happens except that the parents and the teachers make behavioral observations on the child twice a week.

A baseline is another 2 weeks, during which the children on medication are removed from medication and we continue with the biweekly recordings for both those on and—previously on and those off medication.

Next slide.

At the end of this month's period, the children are randomly assigned to either the experimental diet, that is, Dr. Feingold's diet, as described in his book and as slightly modified by us, and a control diet which consisted in this case of a special diet that we concocted, taking account of a number of factors.

For example, we wished to have approximately the same nutrient values in each of the food categories. We wished to have foods which did not overlap with the Feingold diet, so that for example, where butter was used in the Feingold diet, oleomargerine would be used in the control diet. Fried foods were eliminated as a placebo type of device to give some credibility to the diet. And a variety of other food changes which allowed the child to eat the normal complement of foods that would contain the suspected artificial colors and flavors.

We did not in other words load the diet or challenge the children with a special additive loaded diet, but simply allowed the child to eat what he normally would.

We documented the food intake both prior to the study and during the study by having the parents record in the diet diary everything the child ate, weighing the food, and then tabulating the nutrient values and the RDA values according to standard nutritional tables.

Dr. Margan. I have a question on that. As far as the experimental diet you defined as a modified Feingold diet——

Dr. Conners. Yes.

Dr. Margan. The controlled diet in a sense was also a modified Feingold diet, in that it was a diet which was supposedly devoid of any type of additives. Is that correct?

Dr. Conners. No, I am sorry. That is not correct.

Dr. Margan. OK.

Dr. Conners. The control diet is not devoid of additives. It contains——

Dr. Margan. It is the regular type of diet the child might be eating, but you made certain modifications to imply that it was a diet?

Dr. Conners. Right. It was in effect a placebo diet.

Dr. Margan. A placebo diet.

Dr. Conners. Right. It required the parent to shop carefully, to—and so on.

Dr. Margan. OK. This was a social and psychological ritual, but it——

Dr. Conners. Exactly. Right.

Dr. Silbergeld. Were these diets blind to the parents, children and teachers?

Dr. Conners. The diets were not blind to the parents in the sense that they, of course, knew what the child was eating.

Dr. Silbergeld. Did they know it was the Feingold or non-Feingold diet?

Dr. Conners. We ascertained this via questionnaire, and virtually all of the parents had read something about the Feingold diet in the papers, so I would say that they knew that the Feingold diet was the Feingold diet.

The control diet we explained, we simply told the parents that we were studying the effectiveness of two different diets, that either diet might be effective, or that neither diet might be effective, and that we needed to give the child both diets in order to evaluate which was most effective. We explained to them that either might, in fact, produce changes in a positive direction, and that they should be quite objective about that.

Most of the people thought that we were developing a modified new diet for control of hyperactivity, so they were, I think reasonably sold on that.

It was not of course blind in that sense. The teachers also knew that the children were in a dietary experiment. They did not know there were two diets, and the parents were instructed not to communicate with the teachers in this regard. We questioned the teachers after the experiment and they had no knowledge of the specific starting time of the experiment or when the diets were crossed over, or that there was a crossover diet.

The children on the whole I would say were blind in that they had little or no knowledge about the Feingold diet per se. They knew that various foods were being restricted that they often liked, and we tried to balance that in the two diets.

Dr. Cinque. Do you know if any of the children prior to your experiment were previously on a diet to control their hyperactivity?

Dr. Conners. As far as I know, none of the kids in the study had actually been on the diet, although there was one subject whose mother was a nutritionist who had followed the newspaper articles and had tried something like the diet, but without any great detail.

I might add that we gave the parents a very detailed set of instructions, including a detailed list of items to be eliminated, as well as items to substitute, so that they had both an elimination diet and a list from which they could choose acceptable alternative foods.

Dr. Margan. Just to come back, you attempted to disguise the fact—there was no mention, in other words, of the Feingold diet?

Dr. Conners. That is correct.

Dr. Margan. So you said "we have two diets, two experimental diets"——

Dr. Conners. That is right.

Dr. Margan. "And we just want to see which experimental diet might benefit the child more than the other"?

Dr. Conners. Right.

Dr. Margan. Now, in the population that you were dealing with, do you think that this population was sufficiently sophisticated—let us say the mothers preparing this—to in a sense point out or figure out or determine that one of these was the Feingold diet and the other one was not the Feingold diet? As a very high likelihood or as a high probability?

Dr. Conners. Yes, as I said I think it is very likely that most of the parents were aware of the fact that there was a Feingold diet. I mean, many of them came into the office with Dr. Feingold's book in their hand, so it was not a hard problem to figure out the degree of their knowledge.

We did in fact check this with a degree of prior knowledge questionnaire, and found that most of the parents did know.

OK, so after the baseline the children were randomly assigned to the two diets. The parents and the teachers complete the biweekly 10 item behavioral questionnaires for a month, and at the end of that time, I interviewed the parents, and they had been instructed not to discuss specific foods with me. The project coordinator and nutritionist handled all of the dietary and nutritional interactions, including talking to the parents during the week about infractions or, when they would call asking whether a particular food was prescribed and so on—that was all handled independently, and my job was simply to interview the parents and determine from their verbal report, plus the teacher's rating report, an overall clinical, global impression of the degree of change or no change on each of the diets.

So I was blind to the particular diet at the end of 1 month.

Dr. Margan. You did not know which diet they were on?

Dr. Conners. That is correct. The children were assigned by random number table, by the project coordinator, Dr. Goyet (?).

Dr. Cinque. Were the body weights of this population within normal range?

Dr. Conners. Yes. The physical examinations showed the children were within normal limits for body weight and we excluded any children who had any kind of important primary physical problem.

Dr. Margan. I would like to ask one last question, I hope. That is, as far as these two diets were concerned, in terms of the nutrients, were they very carefully followed?

Dr. Conners. Yes. The nutritionist evaluated both the projected diets and the actual intake. I will have some comments on the nutritional differences between the two diets in a few moments.

Dr. Chopra. Was there any history of allergy in any of the subjects of the study?

Dr. Conners. Yes, there was a history of allergy. I do not remember in how many. There were perhaps a quarter of the subjects who had such a history.

This was not, as far as we can tell, related to the outcome at all.

Dr. Kolbye. May I remind people to speak louder so that everybody in the room can hear, please?

Dr. Katz. I would like to know if you have any food record of food intake?

Dr. Conners. The answer is yes, we did keep records of food intake, including the kind of foods and the amount.

Dr. Katz. The amount?

Dr. Conners. Yes.

Dr. Katz. And you followed vitamin intake and so on?

Dr. Conners. Yes. We calculated the percent of recommended daily allowances for all the vitamins, the calories, the carbohydrate, protein and fat composition.

Dr. Mahaffey. Were the children on controlled diets given detailed instructions comparable to the other diets?

Dr. Conners. Yes. The instructions were exactly the same as the other diet, except for the content of the foods. This was very carefully attend to. We were cognizant of the fact that we are dealing not just with a dietary study, but a social-psychological study, so we wanted the set to be comparable for the two groups.

Now, after I interviewed the parents and they gave me their report and I made a global rating, I explained to the parents that regardless of the outcome, the next diet it is important for them to follow. That is, if they had a good outcome, it is possible the next diet could be even better, since no child is actually cured.

If they have had a poor outcome, it is important that they follow the diets just as scrupulously and pay just as much attention to compliance and the other aspects of the child, so that we could make a fair comparison. I stressed the fact that we really did not know which of the two diets might be best for their child, which of course is true, and that they should be just as objective, and so on.

So I tried at that point to offset any problems of carryover from the experience with the first diet by explaining this was a new diet that had to be evaluated in its own right.

Next slide, please.

At that point we had the crossover. The child was then switched to the other diet that he had not had, and the same procedure was followed for another month. The biweekly ratings were continued by the teachers and the parents, and then at the end of the month, I interviewed the parents again.

Now, one important thing in evaluating the information which was not really very clear in my report, I am sorry to say, is that the parent were given the set, as were the teachers, of comparing the child with the previous period. That is, after the first diet, the question was, how does the child compare now with the way he was when you first brought him in? That is, on baseline.

After the second diet, how does he compare now compared to the previous period when you brought the child in? So that the reference point, the psychological reference point for the parent and the teacher is the previous 1-month period.

Dr. **Margan**. I thought you said that the teachers did not know when the diets were begun?

Dr. **Conners**. That is correct. But they were told, "Compare the child against the previous"——

Dr. **Margan**. A certain time?

Dr. **Conners**. Right. It is a 1-month period.

The teachers actually sent in biweekly ratings, but they have to have some standard against which to evaluate it.

Now, in the pilot study in Boston that I mentioned, we contacted those parents 6 months after the initial trial, and if I can have the next slide, I think I have that data. No, I am sorry, I do not.

Essentially, what we found in that followup was that of the eight children, seven were available, and of the seven, six were following the Feingold diet and had elected to follow that diet rather than the control diet.

Of those six, four had shown, according to the parents, complete behavioral improvement. They were no longer symptomatic. Two were showing some behavioral difficulties, and both of those cases were on medication still, but at a reduced dosage compared to the previous trial.

That was, of course, a nonblind followup telephone interview which indicates that there is some suggestion at least of continued benefit. I do not want to spend any time on that, since the value of the open part of the trial is limited.

Now, this shows the response for a particular child, plotted over the 12 weeks of the experiment, the hyperkinesis index being the 10-item scale which has a range from 0 to 30. The top graph shows the results from the parents' reports, and what you see is that a relatively stable high baseline symptomatology, followed by a decrement of symptoms on the K-P or Kaiser Permanente or Feingold diet, followed by a return of symptoms on the control diet.

A similar pattern for the teachers is found in this particular case, and the correlation between the teacher and the parents' ratings is remarkably high. In every case, whether the child improved or not, the symptom ratings seemed to be relatively congruent, so that we had some confidence that we are getting two different observations of the same organism, who exhibits the same behavior that can be detected more or less the same according to the scores.

Dr. **Combs**. May I be clarified on this point? The relative scorings, based on the previous observation period, does this mean that this was a 2-week interval, which is a striking reference point, or is it——

Dr. **Conners**. No.

Dr. **Combs**. Fixed from the beginning of each diet?

Dr. **Connors**. Essentially the instruction is as follows. "When you rate the child, rate him as he is today compared to the way he was when you brought him in to the study."

OK, that would be reference point No. 1. Now, after a month, "Compare the child today as he was when you brought him in at the end of the last period." In other words, compare him with the previous period, the previous end point period.

Now, I do not want to stress that very much, because I think it is a trivial point. In fact, parents use, and teachers use a kind of objective reference.

The scale is on a 4. scale, zero, just a little bit, quite a bit, very much, presence of symptoms. They tend to use an absolute scale, but it is simply a matter of—it is a fine point of grading scale technology to specify where the comparison point is.

In fact, I think they developed a kind of sliding average of their own, an ongoing computation of the child's performance compared to some abstract or previously maintained baseline.

Dr. Combs. This means then that these are not 2-week interval baselines, but at the beginning of each diet period is the reference point?

Dr. Conners. The pretreatment baseline points represent the parents judgment of symtomatology compared to the previous month. The K-P diet points represent the parents' estimate of symptomatology compared to the baseline period.

The control diet period represents the parent and teacher's comparison with the K-P diet period.

Dr. Cinque. On the left-hand column you have "Pretreatment, no medication."

Dr. Conners. This happened to be a child that had not had medication. That is why it was indicated that way.

This child had not been on medication, and that just simply indicates that fact.

Dr. Cinque. How many of the children, of the different children, were on medication prior to the study?

Dr. Conners. I think five or six. I do not recall.

Dr. Cinque. And you tried to explain to them that in the baseline period, as they are taken off medication, an increase in severity——

Dr. Conners. Yes.

And that in fact happens as you will see.

Dr. Chopra. How long did it take for them to respond to the diets?

Dr. Conners. Well, as you can see, our measurement intervals are twice a week, so the finest point we could get would be 2 to 3 days.

You can see that in this particular case, response was in the very next rating period, which would have been within the next 2 or 3 days after the end of the diet.

Now, usually the children started the new period over a weekend. That is, after the baseline, there would be a weekend, and then they would start on the diet. So there is perhaps a 2- to 4-day variation there.

The question cannot really be answered from this data because the measurements are spaced far enough apart we do not have that kind of data.

Dr. Chopra. I was wondering, in your interviews with the parents, did you have any indication that they——

Dr. Conners. Usually if they began to see changes, it was within a few days. It was not a long period of time.

Dr. McNutt. Point of clarification. Are these data for a single child or is this——

Dr. Conners. This is data from a single child. I put it up for illustrative purposes to show you how the baseline of the treatments are examined.

The next slide, please.

Dr. Cinque. Do you have any speculation on why that particular child in the pretreatment period, his hyperkinetic index dropped?

Dr. Conners. May we have that slide again reversed, please?

Dr. Cinque. Both the parents and teachers see a drop in hyperkinesis, and yet he is not on medication or on a diet.

Dr. Conners. Well, I think you would see that the parents' mean is almost exactly the same throughout, if you drew a line through those points, it is pretty stable.

Dr. Margan. What do you think is a significant change?

Dr. Conners. Well, 10 percent is enough to usually pick up a drug effect. The changes here are somewhat larger than that.

Now, the change from the teacher, the drop that you see there, obviously could be any number of things. It could be the child actually did quiet down during that period, as a random fluctuation in his behavior. It could be that it is an initial Hawthorne type of effect of some sort.

But I think it would be hazardous, given the standard error of measurement here, to worry about individual fluctuations. This is typical of single subject baseline data that it shows some fluctuation, and every little fluctuation does not mean a real variation.

Dr. Springer. Springer,- FDA. Is it not true that only out of the nine children who received this, only one or two at most showed at this time any real decrease of symptoms from baseline?

Dr. Conners. That may be correct, Dr. Springer. I really do not remember whether that is the case. You mean, showed that degree of initial——

Dr. Springer. Yes.

Dr. Conners [continuing]. Variability? Yes, I really do not know.

May I have the next slide, please.

This is a child who got the control diet first followed by the K-P diet, and here you see an even larger degree of pretreatment fluctuation. I put that up simply to illustrate the fact that you do have a varying baseline; also, however, if you look at the diet period, you see a rather clear concordance of the changes occurring in the two treatments. Even the baseline is—the parent and teacher scores are correlated with each other. So we think these will measure real changes. They are independent and they are relatively highly correlated.

Next slide, please.

There is the followup study data. We can skip that, since I have already described that to you.

Next slide, please.

Looked at graphically, the percentage of improvement against baseline, now, for the K-P is 15 percent for both parents and teachers, as against roughly 3 percent or less on the control diet.

Next slide, please.

This is a presentation of the mean of the hyperkinesis index scores under the various treatments for the two kinds of graders.

The analysis of that is on the lower half of the table, in which you see that comparing the K-P diet against the baseline, .05 significant improvement on the K-P diet compared to baseline. Control versus baseline, no difference. K-P diet versus the control diet, no difference for parents, a .005 difference for teachers.

Dr. Margan. What was the end?

Dr. Conners. The end is 15.

Dr. Margan. Fifteen.

Dr. Conners. Next slide, please.

This shows the average of the teachers' ratings across the 4 weeks of pretreatment baseline, and the 4 weeks of control and K-P. As you can see, there is some divergence between the two diets in the level of hyperkinesis scores. That of course for the teachers represents, the .005 difference I mentioned represents the average mean difference between the two treatments.

Clearly they are not different in every point there. In a print analysis of variance or something of that sort, looking at the individual points would have shown only that certain of these points are different.

Dr. Silbergeld. What is the mental history of children who might be placed under such studies without any dietary intervention for that period?

Dr. Conners. I think you can see from pretreatment baseline averaged for the 15 subjects that initially, whenever you make some kind of contact, you get an improvement. That tends to level off, and you have a more or less standard baseline, and it will stay that way, over a period of years. Now, as the child gets older, of course, you will see changes.

Dr. Silbergeld. Would either of those lines—if one were able, on the basis of the research that you have done on a great number of children, to extend the baseline as it were for another 4 weeks,—

Dr. Conners. Yes.

Dr. Silbergeld. Would either of those diet effects significantly differ from a baseline extended?

Dr. Conners. You are asking me to predict what would have happened had we done something else. I do not know. If one asked the question in a statistical sense with these data, we know that the control diet does not differ from the baseline diet. We know that a K-P diet does differ from the baseline diet.

Dr. Silbergeld. Well, there is a somewhat difference in terms of the effect of the experiment in its ongoing pattern throughout time, so that it is not entirely—it does not deal entirely with those issues to compare that to another time period.

I was just wondering if, on the basis of the studies that many people have done, Craig and you, if one were to look at the children who have been studied for a rather long period of time over summer vacations, for example, and their behavior for a long baseline period, does it settle around that hyperkinesis index of 15, which is sort of what it looks as though it might——

Dr. Conners. They were selected, by the way, on that criterion.

Dr. Silbergeld. Right. And if it did, would it be different from the K-P diet?

Dr. Conners. As I say, I do not know the answer to that. We did not do a long-term study.

Dr. Margan. Do you have any evidence as to what the noise level is. What is the noise level people observe in hyperkinesis without any treatment.

Dr. CONNERS. Well, the longest we have is, say, 3 to 4 months, and all I can say is it tends to be stable. For example, you look at the placebo group. It tends to be relatively stable after that initial time.

Dr. MARGAN. Plus or minus 10.

Dr. CONNERS. Right.

Next slide. I think that may be the last. OK, if you will turn the slides off and we can have the lights, I will try to wrap up very quickly.

Dr. Lipman, did you have a question?

Dr. FORBES. Is the control diet very readily recognizable as being distinctly different from baselines, or is it a relatively minor departure from normal, the normal type of diet that these children were consuming? The K-P diet is quite obviously recognizably different.

Dr. CONNERS. It is distinctly different. It is easily recognizable, and it involves a lot of problems in followup and to prepare it. We had a questionnaire which measured the degree of dietary difficulty, the extent to which the parent had trouble following the diet and preparing it, and the means on those were almost identical for the two diets, 1.5 and 1. something or other for the other diet. They were very close.

So we think the diets were nearly equivalent in the sense that you are asking.

Children complained equally on both diets about missing things that they were used to, so we thought that that was—we also had an index of compliance, the number of infractions. That was roughly equivalent to the two. There was no difference between them.

Nutritionally we found some interesting things. The Feingold diet depressed vitamin intake across the board, particularly vitamin C, which showed a highly significant difference. The other differences were statistically significant but not, I would say, clinically important.

Despite this, I want to stress the fact that all of the children ended up with much more than the recommended daily allowance of vitamin intake and protein intake and so on. The RDA's were significantly reduced from the baseline for control, while on the Feingold diet, but still above RDA's. That is important.

Carbohydrate intake was also significantly reduced on the Feingold diet, although the absolute amount of that is relatively small.

Dr. WEISS. Did you measure weight at the end of the two different diet periods?

Dr. CONNERS. There was no weight difference, although I did not report those. There was no weight loss in either group, contrary to a report that Gordon Lochaff (?) gave in which he claims that there was a weight loss.

I do not know what the dietary control was, but we spent a lot of time on the phone giving people alternative strategies for maintaing intake.

Dr. KOLBYE. In terms of the dietary history of the children baseline as compared to control, were there any differences detectable in terms of, not total quantity of food or nutrient ingested, but the spacing of ingestion, food ingestion?

In other words, did all the kids eat the same size breakfast at the same time all the time, no matter whether it was baseline control or test diet, or what?

Dr. CONNERS. Well, there was a marked alteration in the percentage of intake of the vitamins and proteins for breakfast. The Feingold diet seems to limit severely the—or not severely, but noticeably, the breakfast intake, so that if you look at it in terms of breakfast intake, the Feingold diet versus the other two periods, there was a difference.

The spacing in the sense over days we did not analyze for. One of the conclusions that we came to and did not stress in the report because it is tangential is that in general the nutritional habits were incredibly poor in this group of kids, and it was obvious that in many ways this represented a singificant intervention in the food habits of the kids.

One child would only eat very limited, specific things, and if he could not have those he would not eat at all. He was a big problem to get to respond.

Dr. KOLBYE. Excuse me. Kolbye again. In terms of the behavioral symptoms, was there any pattern in terms of the times of day or any consistent pattern from child—you know, child to child? Any differences there? Is each child consistent?

Dr. CONNERS. We do not have data on that, Dr. Kolbye. The ratings were done only once per day every other day, essentially, so we do not have a diurnal measure.

Dr. VANDERVEEN. To go back on the diets, you were indicating that there were significant changes in terms of breakfast between the two menus. There are two questions I wish to ask. Did you infer that less calories were consumed on the

Feingold diet? Or did you infer that different nutrients were being consumed?

That is the first question. The second question is, do you, in terms of consumption of the diet, you have indicated there were significant amounts of time spent on the telephone trying to iron out difficulties, et cetera. Was there any difference in consumption of the diet in terms of various food constituents?

Dr. Conners. In terms of the first question, there was no difference in calorie intake, so that obviously there was redistribution of foods.

Dr. Vanderveen. What was higher? What was increased in terms of breakfast? What types of nutrients were increased as opposed to what was being reduced?

Dr. Conners. I am not sure that there was not a difference in calories for breakfast. I do not recall analyzing or looking at it in that way. It may have been done. I simply do not know the answer to that.

But overall the calorie intake was not different between the various conditions.

And your second question?

Dr. Vanderveen. What difficulties—were there significant difficulties in consuming the diet?

Dr. Conners. Both diets presented difficulties. We logged the phone calls from parents; we did not find any difference in the amount of questions. We advised them that at the slightest question to give us a call, because we would rather have you eat the right thing rather than make a mistake. So they would call or we would check with them frequently, and we did not find any difficulties that were different between the two.

As I said, the instrument we devised for that purpose did not show a difference.

Dr. Schain. Did you have any standard instruction you gave to parents regarding telling the children what this was all about? And what was the children's attitude toward this diet?

Dr. Conners. We individually talked to the children ourselves and explained to them that what you eat can affect how you feel and how you behave. That is why we were going to try different ways of eating to see whether it would help them with some of their problems.

The parents gave a variety of their own instructions, but essentially of that nature.

Most kids followed the diets willingly, without very much difficulty. We had various complaints from parents regarding very favorite food items. A kid who had to have a bottle of Coke at breakfast, and so on, did not like the idea of having those removed. But whose were rather specific complaints.

In general, the kids would—most parents amazingly enough said that the child himself was a more rigorous follower of the diet than they were. That is, he would remind: you know, mommy, I am not supposed to have catsup today. So please take it off the table.

A number of the parents commented, that the child was very enthusiastic. A lot of the success of that has to do with the set that you give the parent and the child. I think they were all enthusiastic and perhaps hopeful that it was a meaningful thing to do.

But I think just handing out the diet without instructions leads to difficulty.

Dr. Lipman?

Dr. Lipman. I was wondering if you could comment on the notion of responder and nonresponder. I think Dr. Feingold's hypothesis has to do with the fact that certain children selectively will respond. And also then, if you could say a little bit about the relative percentage of the children who responded, and the relative percentage who might have shown a placebo response. And then how the placebo response in this study would compare with the placebo response in other studies?

Dr. Conners. OK. I should mention an important feature of the outcome which I neglected. That is what the crossover showed that almost all of the kids who responded—in fact, I think it was all of the kids who responded—got the sequence control diet, Feingold diet. So that the response really came in the latter part of the trial for those parents.

I believe it was five of the nine children in that sequence showed a therapeutic response, both globally and by ratings.

So essentially we are talking about 5 of 15 children all or more of whom were into one sequence. Am I correct on that?

The five children then represents 33 percent of the sample. The placebo response in this study has to be judged in terms of the control diet, and there you saw we got roughly a 3-percent plus or minus improvement on the placebo diet.

In fact, there was very little placebo effect from the study.

If you want to count the Hawthorne effect, that is, the initial drop in symptoms from rating 1 to rating 2, which is a well-known phenomenon of this instrument, then I would think you would have to think in terms of 15 percent. So we are talking about a third, roughly, of these kids, compared with a rather smaller number who showed any placebo type improvement.

In our drug studies, from a hundred children, we typically get about 20 to 30 percent who will show a mild to moderate degree of improvement on global ratings.

Almost never do you get a significant or very great improvement on ratings in the placebo group, but 30 percent may show some degree of improvement on rating scales.

Dr. KOLBYE. I think we are going to have to hold off questioning in a few moments. But I would like to ask you just one question, if I may as chairman, do you have any further comments on the differing response due to the sequence of K–P diet, control versus control, K–P diet?

Dr. CONNERS. This is a phenomenon which is not peculiar to this study. We went back and looked at the only crossover that we had done with the drug trials, and found exactly the same phenomenon. That is, the rating of the drug changes is much better when it has been preceded by a placebo period. I interpret that as a contrast effect. The parents have a longer baseline, a longer use of the rating instruments, and they can compare the child—it is essentially, when you are giving the child a placebo, the mother says, Well, yes, he improved maybe a little bit, but when you give the child a drug they say, Wow, now I can really see the difference.

Now, that is in effect the kind of change we got here. That is my interpretation of those data, although others are possible, and I would certainly say that with the problems in random assignment to a small group of 15 subjects, we do not know whether the responders happened to all end up in one group, which would account for the effect, or wether it is a simple contrast phenomenon, which would be another explanation.

Dr. KOLBYE. As an additional question, and I might invite you in a moment to comment about any suggestions you have for research that should be done, and I might mention to the rest of the group that Dr. Conners who is in sort of a dual position here, having completed one piece of work, and proposing some additional studies.

In terms of isolating out the psychosocial factors involved in studies of this nature, do you have any suggestions or recommendations of how future studies should be conducted?

Dr. CONNERS. There are a lot of points to consider, Dr. Kolbye. I will just mention a few. No. 1, I think the screening is essential. Having been in this business for quite a while, it is clear to me that not every child who looks at first glance to be hyperkinetic is what he appears to be.

Our own feeling is that from our research there are definite subgroups of children who have different etiologies. Our approach in suggested studies is to differentiate those at the beginning by both behavioral and physiological methods. For example, we have good reason to suspect that physiological underarousal comprises one subgroup of children. There are methods for differentiating those children.

We have reason to believe that there are genetic family differences in the one group of hyperkinetic children; therefore, that is another basis for subgrouping.

That is point No. 1, the differentiation of the subgroups based upon genetic and physiological characteristics is important.

Point No. 2, we think that an elimination diet by itself compared with the control diet is probably not a satisfactory method for drawing firm conclusions, and propose to do an experiment in which we have a challenge period, inserted between baseline periods.

There are various designs. The one we have chosen for outpatients is essentially A–B, A–B because you want to have the child on and off the diet at least twice.

For residential patients I think this can be shortened, and we have suggested a baseline challenge baseline; if the control of the foodstuffs is completely out of the hands of the institutional staff it is done in effect totally blind.

That design does not, of course, handle a placebo phenomenon. But you do not have a placebo phenomenon if you have objective measuring instruments.

This brings me to the last point, and that is I think that some specific measures above and beyond rating measures tied to the people in the child's environment have to be used. We proposed objective measures such as the actomer(?), measuring actual amount of energy expenditure in the child, time sampling observations of the children in the classroom, and finally some specific allergy testing methods in which food is introduced and blood response is objectively measured.

Dr. Margan. What type of blood response?

Dr. Conners. Well, there are some methods that have been described to me. I am not very familiar with them, in which a wide range of food substances are introduced, and the erythrocyte changes are used to evaluate the allergic potential of those foods.

I will have to defer on that question to the specific nutrionist who is advising us.

I am sorry to take up all of your time.

Dr. Kolbye. Not at all. Thank you very much. Later on we will invite additional comments from you.

I might mention, I neglected to have several people introduced here, also members of the Interagency panel.

Dave, could we start with you?

[General introductions.]

Dr. Kolbye. Then it is a pleasure to introduce Howard Seltzer, who is with the Office of Consumer Affairs, in the Office of the Secretary, HEW, who is joining our Interagency Panel.

At this point, I would like to then shift to—excuse me, is there anybody else on the Interagency Panel that has not been introduced? I do not want to repeat the same mistake twice.

Our next visiting scientist is Dr. Esther Wender, whom I would invite to make any comments or presentations that she wishes, please.

Do you have any slides or need for projection?

Dr. Wender. No.

I believe the committee already has copies of a couple of things that I submitted. One was a brief writeup of a pilot project that we conducted last year, which I will report on very briefly. The second is a research proposal that we have submitted.

I would also like to give you copies of a couple of things, first of all the initial page of the pilot project report, I mean of the research proposal report, has a couple of errors in, minor errors in figures. So if I can pass that around to the members of the committee.

Also in the document that I submitted to you there was obviously some information left out on the sixth page, and I now have that, and I will pass that around to you too.

In the brief amount of time that we have, I would like to just go over very, very quickly, and I will leave a lot of the questions unanswered, some of the findings in the pilot study that we did last year. Then I would like to go on right after that to the question of research design, because I think that is the important issue that this committee should have to address itself to.

I would not like to dwell on the pilot study report, because I would be the first one to say that the information that we obtained on that very low budget study that we did was almost impossible to interpret with any kind of firmness.

Therefore I do not want to spend a lot of time on what we found, because I think it all has to be repeated.

Reading from the research proposal: "11 hyperactive children were placed on Feingold's food additive and salicylate free diet for a period of 4 weeks. For the next 3 weeks, the children remained on the diet while being challenged with either sodium salicylate or an identical placebo.

"Each child served as his own control in a double blind, crossover design. During the first 4 weeks, 7 of the 11 children showed an initial improvement in their hyperactive behavior as measured by questionnaire responses from both parents and teachers.

"The remaining four children showed no improvement. Six of the seven who apparently improved showed a return to baseline levels of behavior sometime during the next 3 weeks of the study.

"These changes bore no consistent relationship to the ingestion of sodium salicylate or placebo, suggesting that the initial response represented a placebo or Hawthorne effect.

"All three patients whose parents chose to continue on the diet at the termination of the study had discontinued the diet at followup 3 months later, suggesting that the parents perceived no continuing beneficial effects."

Well, that is just a terribly brief summary of what we determined in that first pilot study.

One of the questions——

Dr. Weiss. Excuse me. What was the schedule of administration of the sodium salicylate and in what dose?

Dr. Wender. The dose was 150 milligrams per tablet, given twice a day, and that figure was chosen on the basis of our nutritionist's evaluation of the approximate sodium salicylate level that would be found in the consumption in the normal diet, or equivalent kinds of chemicals consumed in the normal diet.

And the schedule was, let us see, during the first 4 weeks was the baseline period on the diet. Then during the fifth week, half of the patients received sodium salicylate; during the sixth week that same half had received placebo, and during the seventh week placebo.

And in the other half of the patients it was just the opposite schedule. During the fifth week they received placebo; during the sixth week they received placebo; and then during the seventh week they received the active medication.

It was a random table assignment to each of those two treatment categories.

Dr. Feingold. What was the purpose of that as the index? What was the justification for it?

Dr. Wender. The justification was that that is one of the items that you would remove from your diet.

I know that when we heard you talk last winter that you felt that that is perhaps not a crucial item in most cases. But at that particular time it is what we had available, and since it was one of the items that was definitely being removed from the diet, we felt it was a reasonable challenge material.

Yes?

Both of them were capsules, and they were prepared by our school of pharmacy to be exactly identical. The placebo contained a——

Dr. Sobotka. I was wondering about that reversal. Was there—how rigid was the attempt to make the children adhere to the diet?

I am wondering whether they might not have shown improvement only because they had gone off the diet.

Dr. Wender. Well, like other people who work in this area, we have tried to document any infractions, diet infractions. All of our patients kept a diet diary. We went through and marked down all the infractions, and then tried to relate that to the changes in behavior, since we could find no relationship between infractions and changes.

Dr. Sobotka. What about after? You mentioned some three patients who had stopped after several months. Were you able to find out whether that might have been the reason that the children——

Dr. Wender. No, that was a phone followup of the sort Dr. Conners described, and we did not go into details at that time. No.

Dr. Margan. There was no baseline? You entered the Feingold diet immediately, and then 4 weeks after they were on the Feingold diet the solicylate was——

Dr. Wender. Well——

Dr. Margan. So in other words, the Hawthorne effect would have appeared for the initial 4 weeks of the Feingold diet?

Dr. Wender. That I considered to be one of the big problems in this study, and as Dr. Silbergeld pointed out, I think that the amount of noise in the system is an extremely difficult thing, and very important to evaluate when you are looking for effects that may be so small that the noise in the system clouds your ability to detect the effect.

We did have a baseline period, but it was not long enough. Initially the baseline period was only a week long. Then it was 2 weeks long. But I am convinced that that is not long enough. I think that baseline period has to be longer in order to try to get a differentiation.

What we propose to do is to make just a few changes in the basic design that was followed in this pilot study.

Dr. Margan. Incidentally, what were the ages of these children?

Dr. Wender. They ranged between 3 and 9 I believe. It is in the report. 3.5—the average age was 7.

The ones that were as young as 3 had to be in some sort of nursery school setting so we could teached evaluations from them.

Dr. Margan. And you used the Conners——

Dr. Wender. Yes, we used the Conners symptom questionnaire.

Dr. Cinque. Did you use full scale or the abbreviated scale?

Dr. Wender. Both. We used the full scale in the initial assessments to establish baseline. We used the abbreviated symptom questionnaire to follow the patients along.

That was an initial problem, because we found that the scores on the 10 items in the abbreviated symptom questionnaire when calculated as they were abstracted from the full questionnaire often yielded a higher score than the score on just the abbreviated symptom questionnaire alone.

Now, again I think as we extend the baseline period, the question as to whether that is a real finding or again just reflects the noise in the system would be better ascertained.

But we tended to find higher scores on the full symptom questionnaire than we did on the abbreviated one alone.

You see what I mean? The full symptom questionnaire, we would extract the ten questions, score them, as compared to what we would get on the abbreviated symptom questionnaire.

Dr Cinque. But you only used the full scale on the initial——

Dr. Wender. That is right. But we also established the baseline on the abbreviated symptom questionnaire. We used both.

Dr. Cinque. Throughout the test period, you used both, is that correct?

Dr. Wender. No. Throughout the test period, we just used the abbreviated symptom questionnaire, but we established the baseline on both.

Dr. Cinque. OK. And then how were you able to project what a full scale would have been later on in the——

Dr. Wender. We could not.

I do not know that. We did not.

That is one thing that we could have done, but we did not.

The changes that we propose in the study to follow, I think the essential changes are as follows: One, we would like to add a time sampling classroom observation to the other measures used in establishing baseline and then in following the children during the diet and during the challenge with placebo and active material.

That is because, again, trying to clarify the noise in the system, we feel we need another measurement, and we feel we need the more objective measurement. We propose to use the O'Leary scale of classroom observation that has been adapted by Rochelle Gilman Klein in her ongoing study of hyperactive children in New York.

This is a time sampling of behavior that is very similar to that reported on the teacher questionnaire; restless and fidgety inseat behavior, out-of-seat behavior, excessive talking, offtask behavior, disruptive behavior, are some of the things that are measured on the O'Leary classroom observation.

The second change is that we would like to extend the baseline period for a longer period of time, and then third, we would like to challenge, not only with salicylate, but with a food coloring and flavoring candy bar, or food item that was discussed at the Nutrition Foundation meeting sponsored last winter that would contain approximately an average daily consumption, an amount equivalent to the average daily consumption of food additives and artificial food flavoring that occurs in the normal American diet.

We would, as Dr. Feingold implied by the question that he asked, he no longer feels that salicylate is probably the important item that has been removed on his diet. He feels that the food colorings and flavorings are probably the offending items. We would like to challenge with that material.

Now, there was some question raised in that meeting as to whether it is possible to develop such a material, and particularly if it is possible to develop a placebo that cannot be distinguished from the material that contains the food colorings and flavorings. But we were assured by the food industry people that it was possible and that, in fact, I believe that the production of such materials has either been completed already or is in the process of being manufactured.

After that, the basic format of the study is the same as the one we did before. That is, half of the patients would receive both the salicylate and the food additive candy bar during the fifth week of the study, followed by 2 weeks of placebo treatment. The other half of the patients would receive 2 weeks of placebo treatment followed by 1 week of treatemnt with the food additive candy bar plus salicylate.

It is my own feeling and the subject of research design that the whole question of control of this particular treatment is terribly important. I feel that it is very, very difficult to control in any other way other than challenging with the material that has been removed from the diet.

I really think that you have to keep in mind when designing the study of Dr. Feingold's hypothesis that his treatment has a very strong potential placebo effect. Dietary changes, particularly in our culture in this period of time, have a very strong potential placebo effect.

The Adelle Davis popularized statement, "You are what you eat" is something that I think is an attitude adopted by the population. The second factor that makes it a strong potential placebo effect is the fact that hyperactivity is seen I think by the lay public as a social disease, and not a medical entity.

As a result, I think all sorts of factors which may impinge upon that particular disorder are going to be picked up and valued highly by most people.

So I think that there really are only a couple of questions that we can answer with good research design. The first question is, Do patients improve?

So far, this is the only question to which Dr. Feingold has addressed himself. Do patients improve? And measuring whether patients improve is something that can be done by following patients with a baseline, and then using objective criteria and then putting them on the diet and following them with these same criteria.

But the second question is, If patients do improve, what is that improvement due to?

Here I feel that an awful lot of the important question that has been raised by Dr. Feingold's statements can be answered by challenging the patient with the materials that have been removed from the diet.

I would suggest these two, salicylate and common food colorings and artificial food flavorings.

If the patients improve, and if when challenged with these materials they do not get worse, they do not return to baseline, then you have the much harder question as to what is the cause for their improvement? What is the reason for their improvement?

I think that is a much harder question to answer.

It is going to take other kinds of research design. But it seems to me that the important answer to, the question to answer first, is this first one, because an awful lot of the social implications of this hypothesis can be cleared out of the way by a research design which will simply answer that question.

Then the other niceties of research design. What kind of subgroups respond better? What might be the cause for response, if needed it is not the salicylates and the food colorings and the flavorings. Those questions can be addressed after this initial question is out of the way.

It seems to me that some of the other methods of control that have been proposed have real serious limitations. The control diet, and a lot of discussion has already taken place on the controlled diet, I think is very difficult to remain blind to, as has been alluded to by many of the questions that have been asked.

Patients become enormously sophisitcated about these things. We have already had the experience in our pilot study, for example, of patients taking the capsules that we gave them, taking them apart, and having everyone in the family sample them to try to figure out which ones are the placebo and which ones are not?

I think that there is a tremendous amount of over-the-counter or across-the-backyard-fence sophistication in the population that cannot be discounted. I would be concerned about a control diet and your ability to really keep patients and investigators blind.

One way to achieve control by one study has been to supply the family with the food items, and another study proposes doing this on an inpatient population in order to control. In both cases the methods are very expensive, and I would suggest that they do not allow still for completely keeping track of whether the patient is taking the offending items or not.

If you are in an institutional setting or the study group has supplied the food that you are supposed to eat, it is still possible to go down to the corner 7-11 and get a candy bar. I think that this has to be taken into account in any kind of study that is designed.

The whole question of documenting compliance is, I think, again a very difficult issue. Dr. Feingold says that he does not worry about the issue of compliance because when these families get better, he feels that they comply voluntarily.

But you have to worry about the fact that after a study has been finished, if patients do not improve, you have to worry about the claim being made that they did not improve because they did not comply with the diet.

But so far in our pilot study and in Dr. Conners' study, there certainly was some improvement noted initially. So I no longer think that is going to be an issue. I think we are going to have a subpopulation that shows some improvement and what we have to determine is what is this due to.

So at the present time I would suggest that we just continue with the diet diary, having the family keep track of infractions, and trying to relate individual infractions to daily behavior, which is what we did in our study.

There are a lot of other things that could be discussed, that I would like to just leave to questions. Those are the two that I thought were important.

We followed Dr. Feingold's diet quite explicitly. As a matter of fact, this is one of the problems, I think. When we tried to develop a diet ourselves with the help of our nutritionist, removing the items that Dr. Feingold says that he removes from the diet, we ran into all kinds of problems.

Because, for one thing there are different forms of salicylate in food. An awful lot of information about what foods contain salicylate and what foods do not is just not available. What kind of artificial food flavorings should be removed is a difficult question to resolve, because some food flavorings are developed from natural sources that occur naturally in foods.

So that we found developing the diet on some sort of independent basis was an extremely difficult thing to do. We begged that question. We simply used the diet as published in his book. Which also excludes any items of caffeine.

Dr. CINQUE. In addition to the diet diary, was any effort made to retrieve uneaten foods during the lunch that was given to the child at school?

Dr. WENDER. During the diet, we insisted that all children, of course, take a lunch to school. You cannot possibly stay on this diet with any degree of reliability and eat the school lunch.

So all children took a lunch to school.

Dr. CINQUE. So essentially the mother's diary is based upon the self-report of the child as to what he ate at lunchtime.

Dr. WENDER. I am sure during lunchtime that would have to be true. That is right.

Dr. VANDERVEEN. I was interested in what examination—have you done any biochemistry on these children prior to their selection? Any blood work? Any evaluation with biochemical—any biochemical assessment of their normality?

And also what dietary information was collected prior to the study? How far back did you go, and what information do you have on their diet history prior to the study?

Dr. WENDER. We had no information except during the baseline period they began to keep the diet diary, so we had an idea, for a two week period of time, what they ate before they started on the diet.

Again, I consider some of these questions, although important, I think they are questions to be answered after the initial basic information is obtained.

Dr. VANDERVEEN. One last question. Why did you decide that the levels of color additives that might be used as a challenge should be held to what would normally be consumed? Why not maybe two or three times the level that you might normally be consumed? Wouldn't that give you a more positive indication?

Dr. WENDER. Well, you know, Dr. Feingold says that just the tiniest of challenges will cause a reversion to former behavior. He states in his book many examples of patients just eating part of a candy bar or a cookie and reverting to former behavior.

So that it seems from the things that he has said that one does not have to deal with a large amount. He would suggest that it is really a very small amount. In other words, it is an ideosyncratic reaction to small amounts of these chemicals.

That is part of the reason.

The other part of the reason is, I do not think we have any information yet about what kind of effects some people might have from excessive amounts.

SPEAKER. I think this is something we should all be aware of; I do not think that any experiments can be justified in using anything higher than the recommended daily allowance.

Dr. COMBS. Dr. Wender, can I clarify your interpretation. As I understand from your summary comments, you indicated that you did have an effect. I am really asking do you feel that you have data that indicates any response at all?

Dr. Wender. The percentage of improvement—you simply take the scores on the questionnaire forms, and the percentage of improvement compared to baseline levels, and you look at that first 4-week period, yes, the patients, the seven that are reported there are patients that improved by 30 percent or more in terms of total improvement from the baseline value.

I consider that significant. It is certainly the extent of the improvement one would see with drug studies.

Dr. McNutt. How do you measure what is the parents' or the teachers' anticipated response on the diet?

Dr. Wender. I wish I knew how to measure that. If I knew how to measure that, I think it would be an interesting thing.

One thing that we have considered very seriously, and I did report it in the research proposal, is the possibility of a control placebo treatment condition as a way of looking at that particular issue. It is suggested that the control placebo treatment condition as a way of looking at that particular issue.

It is suggested that the control placebo treatment condition be placebo megavitamins. In other words, that there be a group that is being treated with megavitamins, but in fact they are a placebo, as a way of trying to generate similar kinds of expectations and then comparing the progress of that particular group with the progress on diet.

But that has been the only method that we could think of that might help answer the question that you have raised.

As I understand it there are a lot of questions that remain unanswered about what is exactly contained in many foods, and particularly the solicylate content.

I am sure that if we decided to focus on the issue it would be possible to do so, but I would suggest that that kind of analysis should wait until a challenge with specific items that are claimed to be removed from the diet before we go on to the more sophisticated technology of analyzing these diets minutely.

I would think that if this proves to be a signficant treatment, that would be an important next step. But I do not think we have answered the question of whether it is a significant treatment.

Dr. Conners. Did you construct the questionnaire to measure the extent to which parents felt food was important in relation to behavior, as kind of a food fad belief questionnaire. And something of that sort, general attitudes towards food and its relationships to behavior I think might be measured.

I think that the strategy of first finding the reaction is important. You can waste a lot of time on the 2,000 additives that one has in the food supply. Then after having identified a putative reaction, there are only eight artificial colors in general use which one could then challenge individually. Then the flavors would be another matter.

But it seems to me that you first would narrow the field by seeing the child who has any response, and then proceeding with individual challenges or replicate the diet challenge itself to eliminate many of the vagaries involved in selecting children who respond to the general inclusion into the food habits of the family.

So our strategy has been really to first identify kids we think are clear reactors, and then I would like to just mention one thing I did not get to. With the actometer measurements, these are tiny devices worn on the wrist and the ankle, we took one of our patients this summer who was a responder, and on 10 consecutive days we measured his daily levels of activity every hour.

On Tuesday and Thursdays we challenged him with a diet which we—not a diet but substances which we thought were high risk, such as things containing yellow flavors and yellow colors. We found a 100-percent increase in activity level in this one child now on both days, within 2 hours after the challenge lunch. It did not occur on any of the other days, which were control days.

I thought that was terribly interesting, although methodologically of course a subject of one in an open trial is—but the data are very clear that for this particular child there was a very specific response.

Now it seems to me that with child it would be possible to go even further and to do one color at a time.

Dr. Katz. I am bothered by something. I am not a child psychiatrist but I wish we could measure something simultaneously addressing both questions, one which would be the behavioral, and the other to be sure of what we are saying instead of introducing something. Having done a little bit of child pharmacology, I wonder if at all possible you could measure maybe in urine samples or whatnot to see is this child complying or not, is the family complying or not? What is he getting?

And you get two answers maybe that you can put one against the other.

The reason I am saying that is that with children and medication, and when everybody thinks that for instance in an institution with adult patients were receiving a drug, and when they came in and measured, you know, the nurse came and gave it to the patients. And when they came in and took blood, there was none in the blood. They went to the institution and they found it all over, so it does not necessarily mean that you know what the compliance is.

Dr. Wender. Again, that is a subject that we discussed at length, in the previous meeting that I alluded to, and although we felt we could measure salicylate we were not sure we could measure it at the levels that it was being consumed in an average diet, but we felt pretty certain that it was going to be very difficult technically to measure these other items in the diet with any degree of accuracy.

I just do not se how it could be done.

Dr. Kolbye. That is the diet. I believe the point was made in terms of monitoring the urine, as I understand the point.

Dr. Wender. No; that is what I mean. Measuring in the urine the metabolytes of these items that are presumably consumed in the diet.

That is what I am referring to.

With the number of items that we are talking about, and the minute quantities in which they may be consumed, I would be very—plus no knowledge really of how they are excreted, how they are metabolized.

Dr. Katz. Well, there are certain things that have been measured, and at least it is something you can put your teeth into.

Dr. Kolbye. I will allow one more question, and then we are running into time problems. Dr. Sobotka?

Dr. Sobotka. I was wondering, were there any children who got worse on the diet? If I might address the same question to Dr. Conners, were there any children that got worse on the Feingold diet?

Dr. Wender. In our experience, no.

Dr. Conners. Not in ours either. We had one spectacular control diet success, and I almost rushed to the publisher with a new diet. But he remitted after a while. But we had no failures in the sense of people actually getting worse.

Dr. Kolbye. Dr. Wender, do you have any additional comments?

Dr. Wender. No.

Dr. Lipman. To clarify, are you proposing now a 7-week study in which the challenge occurs either in the fifth or seventh week?

Dr. Wender. The length of time—there are all sorts of issues that could be discussed.

Dr. Lipman. The 1-week challenge.

Dr. Wender. It is a 1-week challenge, and then the placebo period in between is a washout period because, again, Dr. Feingold says that when behavior is worsened by taking the offending item, it takes a while to reestablish baseline. That is the reason for the week of placebo in between.

Dr. Lipman. I cannot help but ask, Are parents told that it is a 7-week trial?

Yes; they are told that it is a 7-week study. That is something that we have not addressed ourselves to.

Dr. Kolbye. Dr. Wender, thank you very, very much.

I would like to suggest that we press on with Dr. Kerr's presentation, and then break around quarter after 12 for lunch.

Is that suggestion met with accurate rebellion? Can we talk it out for another half hour?

Dr. Kerr, thank you very much for joining us.

Dr. Kerr. I am a pediatrician from the Nutrition Department, Harvard School of Public Health. I am presenting a proposal that has been submitted this morning, and I am sure that you will get copies of it eventually.

We are concerned—the application or the proposal comes from the School of Public Health, and also from two residential schools for children in the Massachusetts Bay area that have extensive experience with the actual management of children with a wide variety of learning problems, including some children who are hyperactive.

I think our concerns are not, because this comes from the School of Public Health, our concerns are not just for the implications of this hypothesis for children who do have hyperkinetic behavior problems, but also for the implications for the total society, because I think the implications of this hypothesis for food processing industries and for the man-on-the-street consumer, including all of us, are very important.

Our interest started about 1 year ago or 1½ years ago, when Dr. Conners introduced our Department and the Landmark School because of an intention at that time to try to evaluate this hypothesis further, and particularly to look at the effects of the diet on food consumption.

We have been chewing on the problem since then, and really a very difficult problem, because we are dealing with something that is extremely personal to most people, which is their food. Most of us have very strong subjective feelings about the relationships of the foods we eat to our own personal health.

It is certainly common to hear testimonials of favorable responses to malignancies and heart disease and arthritis and a wide variety of chronic health problems to an increased amount of specific nutrients or specific foods.

I think we are, all of us, much more concerned about the effects of ways of eating which eliminate foods, or reduce the variety of foods that people have. I think when anyone proposes a diet which eliminates classes of foods or types of foods, or at least changes eating patterns of families, I think nutritionists want to have some assurance that the nutritional risks of this diet do not overweigh or are not more important or aren't more significant than the benefits that are supposed to come from it.

I have really limited ability or limited knowledge of hyperkinetic children. I see a large number of children with growth disorders, and many of them have behavior problems which are of great concern in school and at home. Most of these parents have heard that there is concern nationally about the relationship of things that are added to foods on the behavior of their children.

Some of them and I think this is where my personal worry is, some of them, without supervision, or without any sort of responsible advice, are changing their families' eating pattern in a very marked way. I think this is of real concern. When foods are eliminated for a diet, there must be some way of assuring that the nutrients that were in those foods are still in the foods that are permitted.

I think without some sort of responsible supervision, it is very difficult to achieve this goal. Most physicians and most laymen who advocate elimination diets really have limited competence to do this.

Now, there are a few studies that are being done, and we have heard some of them this morning, that are evaluating the effect of this diet on behavior of children in the real, everyday world where they are going to school, and so on.

We have—we are really, I think, more concerned about three aspects of these studies than I have heard expressed this morning. First of all, I think people who are in the nutrition business are much more aware than most health professionals of the real difficulties of assuring compliance. Even with disorders like diabetes and massive obesity.

The chances of getting someone to really comply with dietary advice is extremely small. We have great worries over the compliance of children of this age, and we all know 6- to 12-year-old children who are away from home for half the day, who eat lunch at school with kids who have another type of food and perhaps more attractive food, who visit other friends after school, who may have a nickel or a dime in their pocket, who have ready access to food vending machines; where their families may be following the diet with meticulous care, I think it is quite another matter altogether to assure that the children involved are doing so.

I just do not see how we can get this assurance on a population that is in the free world.

So we believe that the only way we can look at this effect and assure compliance is by evaluating the diet on children who are in a residential setting, for 24 hours a day, and for several weeks at a time.

There will still be problems. There will still be major problems, but I think the problems will be reduced.

The placebo effect has been mentioned, and we have great concerns over this. Some of the foods—some foods obviously are eliminated from these diets altogether. Others can be made by a family that is motivated to do so.

Now, this making the foods is going to really—may significantly change the psychodynamics in the home situation. And any time the mother and father and the youngster, or whoever, stay home on Saturday morning and bake bread and cookies, you have changed the psychodynamics of that family tremendously.

Now, children respond to changed environments, and they very often respond by changed behavior.

I do not know how you can evaluate this, except, again, in a residential setting where this type of change psychodynamics can be excluded.

The third concern, which seems to—certainly Dr. Conners seems to have approached it—is on the nutritional area.

There are parts of children's diets which are—you might almost call them staple foods—which are eliminated by this dietary approach. Many jams are, many fruits are, hot dogs are, bologana, and there are no exchange—I could not find peanut butter in your book. Is peanut butter allowed?

Dr. **Feingold.** Yes; it is.

Dr. **Kerr.** Ah, because that is—we could be in big trouble if we had to eliminate peanut butter. At any rate, one of our concerns are not so much what the effects of this diet will be on the children with hyperkinesis, although this obviously has to be measured, but we are also concerned about what the effect of the diet will be on the normal siblings of children with this condition, who will by and large be following the same diet at home.

I think when you eliminate foods at home, not necessarily when they are away from home, but if you eliminate foods at home that children are used to and enjoy tremendously, I think you are making big changes that it is very difficult to measure.

Let me tell you a little bit about Landmark School, and I—for any questions about the school or its population, or the facilities, I will refer you to Dr. Drake and Dr. Van der Water, sitting down under the projection booth. They both have extensive experience with treatment of children with this condition, and any questions about the school I will refer to them.

Basically, it is a residential school, 250 children, all with some type of learning problem; 95 percent are male, half of them under 14 years of age. There is no mental retardation. There is no measurable "organic brain disease"; 10 percent of all admissions are on Ritalin or some other psychostimulant medication when they come in. Probably 80 or 90 percent of the children show hyperactive behavior at some time during the day or during some activities.

Ninety of these children between 8 and 13 years of age are isolated—not a good word—are in a separate facility called North Campus; 59 of the 90 have a history of hyperkinesis or a history that is compatible with that descriptive term.

Because of the structured activity in the school, two-thirds of these children now would not be so classified. I think this emphasizes the importance of assuring that the structured—a change in structured activities in a home do not produce the same effect.

At any rate, two-thirds of the children have improved to the point that they would no longer qualify for this term, but there are 22 who are still hyperactive by most anybody's criteria. There are 11 who are hypoactive, of which 8 were previously hyperactive and treated as such by psychostimulant medication.

So at any rate there are between 20 and 30, either 22 or 33 children at this facility. There is also another school, a separate school, and I think it is important that we try to control every single step of this evaluation.

Dr. Silbergeld?

Dr. **Silbergeld.** Are these children who are still hyperactive being treated with any medication?

And the others did not respond to normal medication?

Dr. **Drake.** No; they responded in such a way that they could be taken off the medication.

Dr. **Silbergeld.** And the ones that are still hyperactive did not respond to it?

Dr. **Drake.** Out of the 59, 8 came in medicated with Ritalin, et cetera. Out of those 8 only 2 continue to be on these drug medications. The others were responding positively to the academic environment, and therefore it was felt that the medication was no longer needed. The general principle is to remove a child if it is at all possible.

Dr. **Silbergeld.** How about the ones that are still being rated hyperkinetic?

Dr. **Van der Water.** They are very hyperkinetic.

Dr. **Silbergeld.** And they do not respond to the medication or medication is not used?

Dr. **Drake.** We do not use medication. We get children off medication as quickly as we can.

Dr. Silbergeld. So that question is not relevant in a sense, whether they would respond to it.

Dr. Margan. Are the hyperactive children children who have been there for a shorter period of time, or is there any relation between duration of stay and——

Dr. Drake. They represent a broad spectrum of time. Some have been there for as much as 2 years. Others have been there for 2 months.

Dr. Cinque. What percentage of these have additional counterdiagnostic pathology?

For instance, what is the cause of the institutional placement of these children? Are they very destructive children? Very——

Dr. Drake. No. We have specifically eliminated the traditional pathologies of brain damage, primary emotional disturbance, or mental retardation as being the cause. Our population is described as being of average or high intelligence as measured on the Wechsler or some other test of this type, and they must be emotionally sound enough to want an education and be neurologically intact.

So 80 percent of the cases there is a clear familial pattern of language disability.

Dr. Schain. Why are they in residence?

Dr. Drake. Because of their inability to learn in other school situations. Most of them come from quite a distance because of the unavailability of facilities closer to home.

Dr. Kerr. If I can maybe take 5 minutes to finish this, then I am sure there are some more questions for Dr. Drake. There is another school, and I emphasize the importance of controlling each step, where there is a smaller population of 30 residential students of which 10 would qualify for hyperkinesis.

With these two populations, we think that we can develop objective data on the three main questions we have. One is, Does the K-P diet change activity, either increased or decreased activity, in children who are hyperkinetic or a control group of children, when they are fed either the K-P or control diets?

Second question is, Does this diet, through change in activity, or without change in activity, modify the learning ability of the students and the control group?

The third question would be, Does it have any significant effect on the per capita? We will be unable to measure individual nutrient consumption. I give all credit to anybody who will do this in a family setting on an individual basis, which is very, very difficult.

We cannot do that, but we can measure per capita consumption of all students in the school to see if the specific nutrient and energy intake of the total population changes during the control and experimental diets.

Now, the methodology is described in the protocol that you will get. There are several activity methodologies. No one, I do not believe, has a good handle on how to measure hyperkinesis. There are methodologic problems with each type. We hope to use a variety of types of measures in the hope that either one or a combination may give us data.

We intend to use the self-winding wristwatch that Dr. Conners mentioned. We intend to use a pressure sensitive seat cushion which can measure—or to meaure the frequency of this type of movement.

More important, I think we will be using videotapes of children who are hyperkinetic and controls during specific classes; each tape will be coded by random number and will be evaluated by an individual who is not familiar with either the numbering sequence or the diet sequence.

Now, this can be done because there is one faculty member in the school for each three children. The learning situations occur in a very small area, and the television circuit should be set up so that the groups who consist of control and hyperactive children can be evaluated at the same time.

We want to get subjective data from the parents of these children when they do go home, and half of these children do commute.

We want to get more objective, but still a little subjective data from the teacher. But when you are on a 1-to-3 basis, you become probably much more sensitive to changes in behavior than parents do on a home basis.

Finally, we think it is absolutely essential to have an independent investigator who will in effect live on the compus, or the evaluators will live on the campus, who will not be familiar with the dietary protocol at all, but will be told to evaluate hyperkinetic or control children over the 4-month protocol that we have described.

There is such a group in the Children's Hospital Medical Center in Boston. It is a learning school problem clinic. They see many children for hyperkinesis. They have their own rating protocol for classifying behavior, and for quantifying activity, and we hope it will be possible. They have agreed to participate in this application, but not participate in the application as such, only to participate as a totally independent investigator.

Techniques for measuring learning ability are a specialty of the school. Each child spends a certain amount of time in a tutorial session each day, during which he reads from a very structured book and the number of pages for a given period of time, the number of errors per page are recorded, and can be followed on a longitudinal basis for each child.

The same type of measurements can be done with, I believe, objective quantification of learning abilities through mathematics, through spelling, through finger dexterity tests, and perhaps Dr. Drake will talk more about those when I finish.

As far as the food utilization and food consumption for the school, although it is a rather messy procedure, there are established protocols for doing these, and our Department has previous experience in doing them.

What we are proposing is a series of five sequential 3-week blocks of time, the first of which, and there is a large preliminary phase which is described in the protocol during which the population will be selected, methodology will be standardized, the evaluation forms, and we intend to use Dr. Conners' forms for the parent/teacher evaluations; physical examination, neurologic examination, and so on will be standardized.

The first of the five 3-week blocks of time, and these are consecutive, one will involve the regular school diet. We already know what the school diet is and we know the menus that the kids like, we know what they like for snacks, we know when they eat snacks. The school is 2 miles away from the nearest store. Parents are routinely asked not to send care packages.

There is a soft drink machine but it can be removed, and we believe we can be reasonably certain of compliance. There is always a risk of contraband. There is always. But I think we can do our best. And with the high faculty student ratio, I think we can control that as much as possible.

The first 3-week block of time is the control diet the school is fed. The second 3-week block of time is Dr. Feingold's diet, K-P diet, during which all of the foods which are made in the school, in the kitchen, will be made from basic ingredients. No food colors or flavors will be used, or no menus will be used or no foods will be used unless we can get Dr. Feingold's, I hope, approval to serve as a consultant for this period. I think this is important that we do.

I can anticipate some difficulties, but I think we have to go this step.

The third 3-week block of time will involve identical menus as were offered during the previous 3 weeks, day for day. But during this time we will be using commercial cake mixes. We will be buying bread. We will be buying, wherever possible we will use the menus that are in regular cookbooks, which include synthetic flavorings and synthetic coloring agents. But the diets themselves will not be different as far as the children are concerned.

Finally, the fourth one, the fourth 3-week block of time, is that on the K-P diet, and the fifth 3-week block of time is back on the regular institution diet.

During each of these 3-week blocks of time we will be following each child as an individual to see if his activity behavior changes, his learning ability changes, or food consumption on a per capita basis changes.

We will be able to follow individual children and we will be able to look at them collectively, hyperkinetic versus control children.

We think this will provide the best sort of objective data that we have been able to think up.

I think objective data is really the essence of what we are talking about today. This is really too important an issue to be left at an anecdotal level. We have to really work this out for society.

Thank you.

Dr. Kolbye. Thank you, Dr. Kerr. Are there questions, please?

Dr. Margan. It would appear to me that it would be just virtually impossible for all intents and purposes to do anything blind on this campus. In other words everything, even though you might think that you are doing it, you still obviously are not, because once, you know, that whole thing changes in the kitchen and the whole food changes, et cetera, even your investigator who is not supposed to know what is happening, is going to be perfectly aware of what is happening. All those kids are going to be talking about it.

Dr. KERR. I am sure that this is the real world, that we all appreciate, that it is very difficult to fool people with regards to the food they eat. We hope that by having five sequential 3-week blocks of time we will change the sequential normalty of saying. "Oh, it is a new week," or "This is a new thing that is happening."

We hope that the repetitiveness of these menus will blunt this effect. But it is of obvious concern.

Dr. SOBOTKA. Are the raters going to be eating the same food as the children?

Dr. KERR. Are the raters going to be eating the same diet?

Dr. SOBOTKA. If so, that could introduce a—a hyperkinetic rater——

[Laughter.]

Dr. DRAKE. At the risk of producing paranoia, if this is something that should be controlled we will make them go out to lunch.

Dr. CINQUE. Does the school follow a cafeteria style dining room ordinarily?

Dr. DRAKE. For lunch. For breakfast and dinner we serve family style at the table.

Dr. CINQUE. Family style being that the, whatever is being served is brought to the table?

Dr. DRAKE. That is correct. We do not serve normally onto individual plates.

Dr. CINQUE. Will the test population be isolated in any way?

Dr. DRAKE. No.

Dr. CINQUE. OK. As the child, for lunch let us say, as the child moves down the cafeteria line, he obviously will not have the choice that the other kids in the line will have.

Dr. DRAKE. You see, we have great problems, those of us who have worked for many years with so-called hyperactive children, matching up the children we work with day by day on the one hand with what we read about in the laterature, many times by people who have never worked with hyperactive children, because the child may be quite hyperactive for breakfast and quite hypoactive for dinner, or vice versa.

We have found a positive correlation with weather fronts in the activity level of all children, and this is why we think it is so important that we have a control population under as closed conditions as possible so that in any given day we can not only see what the alleged hyperactive are doing, but what their peers and companions are doing.

Dr. VANDERVEEN. I am interested in what your normal food service is like. What types of food do you normally use in the environment that you have described here? That is the first question.

The second question—well, just answer that one.

Dr. DRAKE. We feel very strongly that the nurturance of food is part of our therapy, and so I have always tried to feed at a very sufficient level with great variety. We make no attempts to control the type of food that is eaten. We do, however, feed the children in midmorning, and they have access to peanut butter, jelly, this kind of thing, after school so that in essence the child may eat as much as six times per day.

We tend to have a higher protein content to our food than most institutions at the present time. Meat or some other high quality protein such as cheese is served at every meal. Children have unlimited access as to quantity.

In the case of the very few obese children who are in our institution, we do provide a table that is low on fats and carbohydrates. A child at any time may ask for, for example, if there is a dietary restriction against pork, all he has to do is to ask the chef for either beef or cheese or some other substance and it is given.

Is this the information that you wanted?

Dr. KERR. Most of or many of the meals are made on the premises from basic ingredients. The chef that is at the school takes great pride in his ability to feed the children well, and is very eager to.

Dr. KOLBYE. I would like to reemphasize that comments have to be preceded by identification and please speak up because it becomes a private conversation rather than a meeting.

Dr. KERR. Dr. Margan. The question was whether the nutritional makeup of the current diet has been analyzed.

We have received 4 months of daily menus from the school. I think we have to get during a control period more specific information, but we do know what the menus are. We do not know quantities yet, and there are some—sometimes the cakes are mixed from cake mixes, which I think would have to be eliminated in a certain part of the study, but also, the chef also makes his cakes on other occasions from basic ingredients in the kitchen.

So the students are familiar with both approaches, and there should be no problem.

Dr. BOESEL. Dr. Wender says that a period of longer than 3 or 4 weeks may be necessary to test for some kind of fadeout (?) effect. Would you adapt your——

Dr. KERR. I have no feeling for this. Obviously it comes down at some point to an economic question. The time is important. We would hope to do this during one of the semesters of the year, and it would have to be designed around the breaks that the children take to go home during the year.

Incidentally, we hope that the children who commute from day to day back and forth will be the best control for the residential students. Their parents at home we believe will use the K-P diet at home as part—because they are very interested in this. But those children will also have ready access to foods which are restricted at school.

So we believe that each aspect of the protocol that we have got is controlled as tightly as we can. Did I answer your question?

Dr. KOLBYE. We will take two more questions, and then we are going to break for lunch. Dr. Lipman?

Dr. LIPMAN. Just a general question. I do not know if you have looked into it yet or not. Massachusetts has recently passed a lot of restrictive laws about some of the research with children in these settings; have you checked to see whether this would be acceptable?

Dr. KERR. No, we have not checked this, and you are quite right, that both—we have a far more restrictive limitation in the School of Public Health, in experimentation involving human subjects. You would have to be passed by the committee, certainly you would have to get informed consent from all of the families. We are really not doing anything. We are not manipulating the children in any way other than changing the diet, but we believe we can do this without any nutritional risk.

Now, whether the children will eat that diet, or whether they will eat enough so that they will avoid a nutritional risk, we do not know.

We do not anticipate problems getting permission, but obviously it is a very important question.

Dr. LIPMAN. I did not understand the rationale for working in two schools. You mentioned that there was another control? Could you explain that?

Dr. KERR. I think we have to control the experiments wherever possible, and I think we would hope to use some of the Linden Hill faculty to evaluate the motion picture studies or the videotape studies from Landmark School and Landmark School faculty to evaluate from Linden Hill.

But we think we will have a purer design if we can use two institutions which are geographically quite remote than if we conduct them all in one study.

We use exactly the same protocol in both.

Dr. COMBS. I would simply like to point out that this would lend itself beautifully to the opportunity of collecting composite samples in an institutional setting, as contrasted to the home, so that if it is necessary to track down certain nutrients, particularly trace elements, which vary, this would give you a very excellent opportunity to do this along the way.

Dr. KERR. Yes. Thank you.

Dr. KOLBYE. I think we ought to break for lunch. There is a cafeteria and a buffet lunch in the basement of the building. The buffet is on the left side of the corridor going down past the entrance to the cafeteria. I would appreciate it if we could return by around 1:15 to start again, and I thank you for bearing with us during this warm morning.

[Thereupon, at 12:20 p.m., a recess was taken until 1:15 p.m.]

AFTERNOON SESSION

Dr. KOLBYE. Our next presentation is going to be by Dr. Harley, from the Department of Neurology, University of Wisconsin. Before he starts I would like to make one brief comment.

We are in receipt of various protocols for proposed research, and for the people in this room not on the committee or not associated with the committee

I simply wish to tell you that we are not privileged to take the protocols and pass them out to anybody; because they do represent a financial interest; they do represent a work product that is proprietary to the investigator.

Dr. Harley has requested that we give him a chance to give the first part of his presentation before questioning, so I would ask that we respect his wishes.

Dr. HARLEY. I have a lot of information to go over, and I think it would be better if we can hold the questions until the end of the presentation.

Approximately a year ago we became interested in the question of food additives and hyperkinesis, and a group of us assembled at the University of Wisconsin got together. There are three pediatric neurologists, Dr. Chunn, Dr. Eichman, and Dr. Tamaze; two other neuropsychologists, Finland and Matthews involved in the project; and one psychologist, Roberta Wraye, plus the dietician.

The project is being funded by the Food Research Institution at the University of Wisconsin.

Ed Traisman is here from the institute with me.

This protocol will be in review similar to the one that we presented at the New York meeting. Some of you attended that meeting last January.

There have been some modifications in that protocol as we have gone along. Initially we proposed the study of 15 children in the spring, 15 children in the fall, in the double blind crossover fashion. Since that time, we have amended the protocol to—we have studied now 11 chlidren in the spring, 10 children in the summer, younger children in the summer, and we are currently studying 27 children this fall.

Our criteria for admission to the project, similar to Dr. Conners, you have to have a rating on the Conners short 10 item parent-teacher rating scale of 2 or greater, or 20. I believe his was 1.5.

Then we also—these are all male children between the ages of 6 to 12. Also, we want a diagnosis—we would like to have a diagnosis of hyperkinesis or hyperkinetic syndrome from the pediatrician.

Now, any two of the above three, that is, parent, teacher, or physician—if any two of those are met, then they are in the project, they meet the criteria for the project.

The schedule in the spring and the summer groups was 2 weeks of baseline, 3 weeks of diet, crossed over to the other diet for 3 weeks, 2 weeks of baseline, then the K-P diet, then the control diet, or vice versa.

In the fall sample, we have 4 weeks of diet versus the 3 weeks in the other two previous samples. The diet, something that we have not talked about is a little different—we have—it has been repeatedly brought up here, the difficulty of compliance in these types of studies—tried to get around that and to alleviate that as best as possible. We go out to the family, the dietician goes out to the family's house, works out a diet, determines the diet history from the family and from, usually, the mother.

Then we ask the family to remove all food from the kitchen area.

Dr. KOLBYE. Excuse me. This information they are handing me does not contain anything in the nature of proposals to discuss what is going on, so there should be no objection to handing them out——

Dr. HARLEY. I have no objection.

We then provide all the food for the entire family, not just the child but for the whole family. We determined the dietary needs, the quantity, food preferences, and so on. Then we provide all that food for the diet period, either a 6-week period or an 8-week period in this fall.

Now, we do some other things to insure keeping the family blind to the various diets. First of all, I tell them that we are investigating diet and behavior, and that they will be on various diets throughout this period of time. We do not tell them they will be on two diets. We tell them that they will have food delivered on a weekly basis to their house; then they can make the leap and assume that possibly each week it could be different.

There are also pseudomanipulations made in the diet. That is, we introduce and withdraw certain foods that are permissible on both diets. For example, sweet potato; certain hot dogs that we have; one week they will have hot dogs in the diet, the next week they will not, the next week they will. The family might then think this is a good diet or a K-P diet, and—when in actuality it does not make any difference. These foods are allowed on both diets.

We also now run into the problem that in school you have birthday treats. So what we do is, if any child has a birthday during the dietary period of the study, we make arrangements to provide all the dietary snacks for the entire class.

If any other child in his classroom or her classroom has a birthday, we will provide the treats for the class. The teacher or the parent, all they have to do is call our dietician, call our staff, and we will deliver the food to the class.

Again this insures that we have maximal control over the diet of the child.

We have also been able to elicit cooperation from several food manufacturers in the production of food items that contain natural and their regular synthetic products. These Nestle candy bars and Twinkies in particular were developed with synthetic and natural substances. This was under the supervision of Ed Traisman who went out to the plant and watched them shut everything down. They produced then box A and box B of food items and delivered all of these thousands of units to the Food Research Institute.

So again the child may be receiving candy bars in a given period of time, and a lot of parents have the notion that candy bars are bad or junk food, and then other times they will give them a candy bar which does not contain any kind of artificial or synthetic constituents.

But again, in their eye it might be bad.

At the end of each week, each dietary week, the dietician goes to the home of the child and reviews the dietary record with the family, with the mother, whoever is taking the dietary record. We also are keeping track of amount of food and types of food that the child eats.

Now, the data that we are collecting, we initially do a physical exam, a neurological exam, looking for soft signs; we do an awake and asleep EEG. We do standard blood and urine work. We also are looking at lead levels in these children.

Then we give a neuropsych battery of tests, including the Wisk, Knox Cubes, short-term memory tasks, some tests of motor and manual dexterity like finger tapping and pegs and coordination, steadiness measures.

Then we have some laboratory tests or laboratory measures of attention and concentration, including standard reaction time paradigms and the continuous performance tasks which some of you may be aware of. It is a rapid presentation of visual stimuli; letters come on the screen and the child has to respond to the letter X or the letter X if it is preceded by the letter A.

Now, during those two tasks we also monitor the psychophysiological state of the child. We record heart rate, respiration, bilateral skin conductance and bilateral EMG.

Again, we want to look at now another dimension of these children and see if in our analysis of the data we can form subgroups of, I think everybody would agree, rather—this rather heterogeneous population of hyperactive children.

The scales that we obtain on a—many of these measures now, these measures—the psychophysiological measures, the neuropsych measures—are obtained at baseline and at crossover and at the end of the second diet.

Now, the measures that we are obtaining on a weekly basis include the parent rating scale—actually at those three times they are giving the parent the long form Conners questionnaire and at the weeks in between the major points, we are getting the short forms, the 10 item questionnaire.

We are getting the teacher long form on a weekly basis throughout the study. I guess that takes care of it for the rating scales.

Another aspect of the project we think is very significant and important—we see the need for an outside or a more objective type of rating, and we get this from going into the classroom and making behavioral observations on a twice a week basis in the classroom.

We have trained observers that go in the classroom with a device that has a keyboard arrangement, and we code data for 20 to 40 minutes on a given child, including on-off task behavior, disruption, gross motor activity, inattention.

These are sort of the broad basic categories we are looking at.

Now, each of the raters that go in the classroom are blind to the study. Everybody obviously that is involved in the project is totally blind, but the raters in the classroom observation are also blind to the fact that this is even a study dealing with diet and behavior. They are just told to go out to the classroom and observe the behavior of children.

They also observe in addition to the child that is in the project, which they do not know, they observe another child, a control subject. This is a control subject that has been identified to us by the teacher so the observers go to the classroom and are told to watch this child and this child.

Now we have some type of control for type of classroom teacher, setting, time of day, tasks going on, age, sex—that we can get an idea of the level of activity or his attention in relationship to what other kids are doing in the classroom in the same period of time.

Now, in the fall sample, we have carried this a little bit further. The question I believe was raised a little bit earlier, what happens when we—if you would look at this over a long period of time. That is, what is the norm? What does normative data look like over this dietary period?

We have identified a number of control subjects now that the parents and the teacher will be filling out behavior check lists on these children throughout baseline and the dietary period.

In addition, we will be getting the observer ratings in the classroom. So that will give us an idea of how do parents of children that they consider to be free of the symptoms classically associated with hyperactive children—how do they view their behavior over a 10-week study period. And how does the teacher see a child over that 10-week period of time?

We also have a standardized situation to make the data comparable on all children because we are involved obviously in many different schools and many different teachers and situations. So in order to have some kind of a common basis for comparing children, we have a grid room observation, where we videotape the behavior of all the children in a situation where you have four identical tables and items on the table. We videotape their behavior and then we score that in terms of their behavior in that standardized situation.

Again, we are going to look at the children involved in the project, and also controlled children. Now, these controls are the same controls that the teacher is rating, their parents are rating, and we are observing in the classroom.

We have completed the spring project; we have completed the summer project obviously. We are now in the process of the fall sample of 27 children.

We anticipate completion of our project December 5, or the first week or two in December.

I will be glad to entertain any questions now.

Dr. Schain. Did you say that, the hyperactive children, are they identified initially in some cases on the basis of observers in the classroom?

Dr. Harley. No. Just the control group. We have to ask the teacher to identify a child that is of equal ability in the classroom that does not demonstrate any types of these behaviors that we are interested in, distractability, inattention, fidgets.

Dr. Schain. The hyperactive children are self referred on the basis of parental concern?

Dr. Harley. Correct. They come via that way; we see people in our laboratory that are hyperactive. We get referrals from pediatricians in the community.

Dr. Lipman. Is that standardized behavior rating which is videotaped controlled in terms of time since the child has eaten, a specific time during the day, or * * *

Dr. Harley. No; it is not.

Dr. Vanderveen. You mentioned that you have standard blood and urine workup on these children, and have you any information as to this?

Dr. Harley. The analyses to date have not been indicative of anything that you would not expect in the normal sample.

Dr. Vanderveen. What type are you making?

Dr. Harley. Again, this is not my area; these are just standard blood—just standard, routine blood analyses. Also lead determinations have been at levels, subnormal levels.

Dr. Kolbye. Subnormal. Could you state what microgram level you are talking about?

Dr. Harley. I believe it is 5.

Dr. Weiss. Where does this come from, that they have a 5 microgram percent lead level?

Dr. Harley. They come from Madison.

Dr. Weiss. Where is the lead analysis done?

Dr. Harley. It is done at the university; there is an individual that does lead analyses there. I can give you his name. I do not have his name.

Dr. Kolbye. Have those circles been cross checked with another laboratory?

Dr. Harley. No; they have not.

Dr. Mahaffey. These are low, but in a large group in Iowa, the results, we found an average of 9, with a standard deviation of 3. So it is not impossible.

They are low.

Dr. FORBES. Dr. Harley, do I understand you are in the middle of your data analysis, at this point in time, and you simply have no preliminary results to hear from your spring and summer studies?

Dr. HARLEY. Correct, correct.

Dr. VANDERVEEN. You have not broken code yet?

Dr. HARLEY. No. We feel it is important to remain blind until all the data is collected.

Dr. MARGAN. On this question, and I am sorry, I think you have probably discussed this before, but how are you measuring to determine compliance? What is your technique?

Dr. KOLBYE. Can you repeat the question?

Dr. MARGAN. Yes; the question was, How are you determining compliance?

Dr. HARLEY. The compliance factor is handled—we try to assure the greatest amount of compliance by the design of the experiments, first of all. I believe I went through those items.

Then we go through the diet battery with the family on a weekly basis. Now, it has been our experience, and encouragingly so that the children take a very active role in the project. They are very enthusiastic about the project. Maybe this has been turned around, we talk about all the psychosocial factors which are very strong in this type of project. Now they are sort of the star of the family; they are no longer the black sheep. Everything sort of centers around them. They are being taken over to the hospital and all these things are being done to them, and the whole family now is revolving around that single child.

Dr. MARGAN. One of the most important of the entire psychosocial factors I would say is this in almost any of these therapeutic diets.

Dr. HARLEY. Yes; if we can get at that some way. And the compliance has not, obviously there are infractions of the diet. You cannot expect, working with children, not to have those.

We try to do everything we can to eliminate even the possibility, and then we stress—we have a number of meetings with the families, and we try to really emphasize how important it is not to have infractions in the diet. Then we say, worse than that is if you have infractions and you do not tell us. We need those reported.

We keep very good tabs on that and we reinforce everything we can to get a good dietary record.

Like I said, our experience has been, one, that not the child takes a negative attitude and goes out to se how much he can get away with, to sneak around, but rather just the opposite. "Mother, I should not have this" or "I cannot have this." And they demonstrate a lot of self-control.

Dr. MARGAN. In fact I would like to question you further on that, because we have heard today that in certain experiments there seems to be some alteration, either in eating habits or the amount of food.

Dr. KOLBYE. Can you stand up please?

Dr. MARGAN. I was just saying that I am interested in this because we heard this morning that in some of the experiments there seems to be an alteration in the eating patterns of the children who are on the Feingold diet. I was wondering what your experience is, because one would expect that very often with this type of psychosocial focus, exactly the opposite might take place, or at least no significant change, or maybe an improvement in the actual eating and dietary habits, if the diet is prescribed properly.

I was wondering what your experience has been.

Dr. HARLEY. I know for a fact that the dietary habits of the family have improved remarkably. They—that is what impresses you most when you talk to the parents. They say at the end of the study, "You gave us so much food, you know, we had more food than we can possibly use." You know, we sort of overwhelmed them with food. I mean, you are literally cleaning out their kitchen. We literally take everything out and we provide from the bottom up. The only thing we do not provide is milk and bread, and we specify what types of bread are allowed.

That is the only thing they do not have to purchase.

They say, "Boy, you know, my husband is eating things that he would never touch before, and the family is starting to eat new things." We give them diets to follow, suggested diets; they are told that they can eat anything that is in the house now. And then we come and remove anything at the end of that week and we go through a lot of true manipulations and pseudomanipulations. You cannot go in at the end of 4 weeks and take everything out and then put stuff in, so we are doing this all along.

Dr. Katz. Who pays for the food?

Dr. Harley. The Food Research Institute, Ed Traisman.

Dr. Traisman. I am sorry. I did not hear the question.

Dr. Harley. She was asking who pays for the food?

Dr. Katz. Does the family pay for the food?

Dr. Traisman. No; it is all funded by the Food Research Institute, of the university.

Dr. Katz. So the child becomes—the family is saving money.

Dr. Harley. That is a large incentive. The parents are asked to do a lot of things. I do not think—I might say, I do not think any of the parents, or very, very few, are in the project and participating in the project because they need food.

We have, the people that have been involved in the project are—many of them in the Madison community are upper middle class individuals participating in the interests of the children.

Dr. Traisman. I would like to bring up a detail on compliance. Since at any time the youngster can eat anything that is in the house, I think this helps to minimize noncompliance, because we remove the foods that are off the diet at every change, so that at any time during the course of this experiment, that youngster can eat anything in that house.

This of course poses the problem of what he is going to do when he leaves home, but we do not know what we can do about that.

Dr. Chopra. I wanted to find out if you had any parents discontinue the study? You know, you had so many children. Are they continuing this up until December, or did you have some parents who decided that they could not carry on with all this?

Dr. Harley. You mean people who have dropped out during the study?

Dr. Chopra. During the study. Do you have any?

Dr. Harley. OK. The question is. In our spring sample and our summer sample, or in the fall now, have we had anybody drop out, anybody that could not follow the diet, they got such adverse reactions that they had to drop from the study. No; we have not.

When they initially presented our proposal in New York, our first design was one of taking children either not on medication, or if they were on medication, maintaining their regime. Everybody said maybe you do not have to do that, and if they are on medication you can take them off without any serious effects.

We have found that to be the case. Obviously, there are lots of apprehensions of the parents and of the teachers in taking a child that is on, and sometimes pretty substantial doses of Ritalin and the like—we have taken those children off with the understanding that if their behavior becomes such that their pediatrician or the staff or the parents, teacher, feel like they should be put back on the drugs, we will do that. But in no case did we have to put any children back on medication.

Now, we have not—we are still blind to the study; we have not analyzed any of the data. It is all being collected. Much of the data is being collected on the standard ECDU package. And the rest of the data is being coded in that format and will be analyzed at ECDU and the State lab. I might say that we have had reports of dramatic effects, good positive effects. We have also had reports of negative effects, severe cases of disruptive behavior at school and at home, very severe disruptions.

Now, let me hasten to add, I do not know which diet they are on, OK. They may be on the Feingold diet, or vice versa. But we have had reports, and I have not collected this in any systematic fashion. These are just parents in the debriefing, or a teacher, when I go out to the school may say, "What has happened to this kid?", either good or bad, you know, great, or "What has happened to this kid? What have you done to him?"

I do not know what diet they are on. All right? But we are getting changes.

Dr. Schain. Are you repeating your measures of attention and neuropsychological measures each time you switch the treatment intervention?

Dr. Harley. Correct. We gathered them at baseline and at the crossovers.

Dr. Schain. Now, are you worried about the practice effects?

Dr. Harley. Yes.

Dr. Schain. What do you think about that?

Dr. Harley. It would be nice to have another group of children that would go through the same, you know, sort of follow through. That is what we are trying to do in the fall. I do not know if we are going to have enough children so that it is going to be a worthwhile statistical comparison. But we will have to take into account and deal with practice effects, things like attention, the continuous performance task, reaction time—everybody knows there are going to be practice effects. But it is a counterbalance design. That takes care of some of it.

Dr. Schain. It is a big headache, because——

Dr. Harley. I know it; we are very well aware of that.

Dr. Wender. The criteria for inclusion into your studies seem to be primarily behavior, questionnaire kind of information, and then you're following children with neuropsychological and physiological measures.

You do not have any cutoff criteria or score for inclusion on the basis of your neuropsychological or physiological variables?

Dr. Harley. No; we do not. Except, I might add, an IQ of 85, equal to or greater than.

Dr. Wender. Because it will be hard to follow changes, you know measure it, if you do not know whether the baselines extend in to—you can only show changes relative to where you started rather than any kind of—in other words, you may be following children who have no abnormality on those measures.

Dr. Harley. Correct. But you can look at the baseline in the diet. The diets compared, contrasted with one another, and the diets compared, contrasted with the baseline. I think that is important.

You are talking—I believe—you do not know what those measures are in a normal——

Dr. Wender. In an absolute level.

Dr. Harley. No; we do not have with absolutes, that is right. We do not have absolute comparisons or absolute numbers that we can refer back to.

We are looking at, we are interested in any kinds of effects related to the diets, to see if some of the notions, specifically in psychophysiological terms of whether or not some of these children, there might be a subset that is hypoaroused in terms of CNS activity.

We did not use any of those measures in terms of criteria. Maybe future studies, other investigations, you will want to set up a situation where you can videotape the child, use a grid room activity level, psychophysiological levels. I think we are still a ways away from that, and how to best combine all those various measures and then end up with a definition of, this is a "true"—we hear that all the time—"true hyperactive child."

Dr. Cinque. Is your videotaping on a daily basis randomly executed? Or what happens? What schedule do you follow for videotaping?

Dr. Harley. The videotaping is done in the laboratory. That is done before baseline, prebaseline, because one of the things that has been observed in grid room observation of children is that there is a tremendous habituation effect. So the first period is sort of a throwaway, if you wish.

Then you have the true baseline, and then you have the crossover and then the end of the diet.

So they come in four times, and the first one you just use for habituation to it.

Dr. Kolbye. Excuse me. Anybody on the other side of the room who wishes to ask a question. I would like to beg your indulgence now. Please stand up every time you speak, because we are missing most of it.

Dr. Cinque. So during the course of the day, you bring the child into the laboratory——

Dr. Harley. I am sorry. There are four points in the time frame of the study. The study is 10 weeks long. You bring him in before the study really starts for habituation. You bring him in baseline, and then a crossover, and then at the end. Three times.

Dr. Cinque. Is the videotaping done over these three periods at the same time of day—or I think the question was asked before, but I was not clear on the answer—is it done after lunch, before lunch, et cetera?

Dr. Harley. Right. The schedule is such that we cannot—bear in mind now the logistics of the project. You have the child that is attending school, and we are making behavioral observations in the classroom at least twice a week. In some cases more, but a minimum of twice a week we have to observe the child.

We also have to bring them back for all the testing that we do thorughout that 12-week period of time. We also have to bring him to the grid room.

Now, it would be nice, and I wish we could have the luxury of time. That is our biggest problem in this kind of project, and anybody that gets involved in this can see it very quickly.

We start talking about a block of time, or so many weeks on this diet, and so many weeks on that diet—put that into a real calendar, with vacations and holidays, and you will find that it is very hard to put the blocks of time that we are talking about as a minimal requirement.

So we have not—we have all that data, but we have not systematically said, we will observe each child after lunch, each child after breakfast.

Dr. Kolbye. Dr. Harley, would you care to make some comments about your proposed—any additional work that you are considering?

Dr. Harley. Yes. We now are obviously ending completion of this project, and we feel as others have discussed that a project done in an institution will afford us greater control and a better handle on the whole dietary compliance issue.

We have looked into an institution in Madison that has very severely and profoundly retarded children, that hyperkinesis is quite a major symptom in their behavior.

Now, we have a sample of 50—there's two wards, 20 to 25 on each ward, so we have 40 to 50 children that have a series or various types of CNS, significant CNS defects. But they all, or 90 percent I believe, are very hyperactive children. We would like to take this population and now alleviate some of the problems in terms of dietary control. Here we have a diet that we can control through the kitchen, residential programs, that are not going to go home. I think in many cases these parents are relieved when you say, "Your child is in this study and he will need to be here for 2 months, 3 months, and cannot go home." I think that releases some of their guilty feelings and they say "Fine."

This is a project that we think affords us some better control—it is a totally different population now than what we are talking about, obviously.

Dr. Silbergeld. What was the rationale of changing from one of the—this description of population to an institutionalized group with significant disorder and retardation?

Dr. Harley. Another test of the hypothesis. I think one thing that came out of the New York meeting, we all agreed upon, that there is not going to be one single study. There is not going to be one single project or one type of protocol that is going to resolve this issue. I think this is a different population. The hyperactivity is a very significant part of their behavior, and we have very, very tight, strict dietary control now in this population. We can observe the effects of the diet, and we can also now take this population and do subtraction studies: instead of introducing and doing challenge types of experiments, we can do subtraction studies of systematically eliminating various synthetic food dyes and colors.

Dr. Forbes. At the end of this study, in December, how many children will you have studied under the same protocol altogether in the three seasons?

Dr. Harley. We will have a total of 48 subjects.

Dr. Forbes. Forty-eight? And one other question—

Dr. Harley. May I just add something?

Dr. Forbes. Yes, sure.

Dr. Harley. The children in the spring and in the fall are male children between the ages of 6 to 12. In the summer we did a younger age group, so we are talking about children between the ages of 3 to 6.

Dr. Forbes. Right. The second question, I would like to ask, is your—the confectionaries that you have produced with and without food colors and flavors, are these conventional amounts of flavors and colors, or are they higher than would customarily be used in such products?

Dr. Harley. Two products, your basic, regular, everyday Twinkie you buy on the shelf, and then the Twinkie made without the synthetics. Okay. So you are using, maybe vanilla now instead of the synthetic.

Dr. Forbes. Yes. So the quantities when present are conventional amounts?

Dr. Harley. Oh, yes. We are not adding anything. These are standard, you know, off-the-shelf products.

Dr. Kolbye. One last question from Dr. Conners.

Dr. Conners. How many children did you screen in order to get the 48 children you have in the sample?

Dr. Harley. I do not know that number offhand. It was a lot. We—I do not know. I am very curious about the incidence figures of hyperactivity, ranging anywhere from 2 to 3, in some cases up to 20 percent.

I believe I have contacted, and every pediatrican in Madison is familiar with the project; we have got all the referrals. I have done an investigation of, a little inquiry of how many patients they think in their practice are hyperactive, and how many are on medication.

Dr. **Conners.** I do not think it is a question of population and so forth, but how many did you initially take as referred and then eliminate on the basis of diagnostic selection to end up with your sample?

Dr. **Harley.** I do not have the numbers for the spring or the summer. I can tell you for the fall. We have had over 100, probably around 100, 110 that we finally ended up with 27.

Dr. **Schain.** What caused exclusion of children from your study?

Dr. **Harley.** Well, if they did not meet any of the criteria, that is, we then asked the parent to fill out the questionnaire, and they did not rate their child high enough on the questionnaire. If the parent did then we called the teacher, and if the teacher did not rate him high enough. If we contacted the physician and he said, "No; the child is not hyperactive," that would—unless the other two are positive.

Dr. **Springer.** I would like to get you to comment on the rationale of using institutionalized children where, presumably, there is some neurological basis or known etiology, in these hyperactive syndromes—according to, I think some of Dr. Conners' work, the improvements on the diet, those who show the most improvement are those that, where you cannot find a neurological basis.

Dr. **Harley.** The reason we went with this sample is that this is a population that shows—we are not saying this is the same group of people. I mean, we are in no way saying that these hyperactive children are equal to those hyperactive children.

Dr. **Springer.** You do not know whether you would expect this much improvement or not?

Dr. **Harley.** Right. Right. And we are not predicting that we are going to find—you know, you would predict you are going to find improvements, and you make the obvious hypotheses. But we are not expecting dramatic or no improvement because these are children with significant CNS deficits.

Dr. **Kolbye.** Thank you, Dr. Harley; we appreciate your presentation. At this point we would like to move to Dr. Schain. Are you set up with your lantern slides? Do you have somebody to work the machine?

Dr. **Schain.** I think so.

Thank you, Dr. Kolbye.

I think I should say a few words about how I got into this business in the first place. I run a pediatric neurology unit at UCLA, and my initial interest in hyperactivity was a sort of self-defense mechanism because of the numbers of children with hyperactive behavior disorders that were referred to our clinic in the pediatric clinics of UCLA, of which our pediatric neurology clinic is a unit.

For a number of years I have been—and my group, when I say "I," I am referring to myself and my two collaborators, Dr. Barbara Keogh(?) and Dr. Judy Margolis. We have been interested in the issue of hyperactivity—interested in the concept that hyperactvity is based on a disturbance of attention, an "attentional deficit" syndrome, a term that was coined, I think, by Roscoe Dikeman a few years ago.

We have been engaged in a search for techniques to measure the attentional disorder that we believe is present in many hyperactive children. We have been studying hyperactive children, and we have also been looking at the effects of drugs on the attentional disorder present in hyperactive children, and I am very impressed by the need to obtain objective measures of behavioral disturbance in children labeled as hyperactive in order to supplement rating scales, because of all the difficulties of rating scales that have been discussed today.

My interest in the question of the Feingold diet came about as a result of a meeting with Dr. Ben Feingold on an airplane back from New York this year at the annual convention on learning disabilities, which I attended for varying reasons. But after discussing his current hypothesis, both on the plane and at a later time, I became persuaded myself that this was a reasonable concept. I could easily envision artificial food additives as producing CNS dysfunction which might manifest itself as a hyperactive behavior disorder, which seemed to me to be very nonspecific kind of response of the central nervous system to a whole variety of adverse circumstances.

And I should state right at the moment that I do not have any data that I am going to report, and I appreciate being invited to present my concepts and the approach that we have developed, which as I said, is mainly based on studies of measure of attention and attentional behavior in hyperactive children.

The study that we have proposed to carry out is, in many ways, not dissimilar from the studies that have been previously described here. I do not think there is any necessity for me to go into details about it, but rather I would like to emphasize what may be unique about our study.

We are interested in studying a group of children. We have entered 40, and we would like to collect the usual kinds of behavioral ratings, psychometric data, and initial neurological examination that has been previously described.

We would then like to subject half of this group to the Feingold diet, and we are, after talking with Ben Feingold a bit, it appeared to us that the K-P 2 diet is the diet that he is mainly interested in at the present time. I feel strongly that the original concept of Feingold's, and the kinds of experiences that he made his observations on, should be the basis of investigations at this time, before going on to trying to identify more specific details of what the active principles might be that have been deleted from the diet.

We—I have not been quite as much concerned with the issue of controls, because we are relying on our measures of attentional behavior much more than we are on rating scales, for assessment of the effects of the diet on behavior.

However, I have been under considerable pressures to have some sort of controls introduced into the diet. I was interested that Dr. Wender mentioned niacin as a contrasting study, perhaps not as a control study, or a high niacin intake, because it has been proposed that high doses of niacin amide may have some favorable effects on behavioral disorders in children as well as, and this has been extended to hyperactive children—control studies that have been carried out have shown the effect of niacin to be not demonstrable, and I regard it as essentially a placebo.

But I have the idea that our two contrasting interventions can be a high dose daily niacin amide intake, 20 milligrams per pound per day is what we came upon—versus the Feingold diet. This is at least a dietary intervention that can be contrasted to the Feingold diet, and I believe that if similar effects are found with the use of either therapy we can assume that improvement is related to factors other than the naure of the dietary intervention.

On the other hand, if there is a significant difference between the two, then that would support one or the other. As I said, I think the niacin amide diet probably can be regarded as a placebo as far as nutritional alteration is concerned.

We would like to start half our group on the high dose niacin amide diet, and the other half on the Feingold K-P 2 diet, and after 6 weeks have a crossover.

Meanwhile, we will test the children in this diet on the various items in our protocol; the main one of which is our battery of attentional measures. If I can have the first slide, please this shows the battery that we have been using for a couple of years in looking at the effects of methylphenidate on hyperactivity. This is the four measures that we are using. The matching familiar figures test, is a measure that will be familiar to those of you who follow cognitive style theory, a device developed by Kagin that has been used extensively, and which is believed in some way gets at the issue of impulsivity, reflectivity kinds of behavior in children.

Impulsive children react quickly and make many errors; reflective children have a long latency of response and make fewer errors. This is not an absolute dichotomy, but holds true in many children. This test separates these two groups, and we have been using it in looking at attentional performance in hyperactive children.

If I can have the next slide, but hold that first one, because we will go back to it in a moment, that is just a sample of the Kagin test, and what needs to be done. Last time I showed this is was reversed, and I gave the wrong answer, so I had better look this time. But the sample figure is the figure on the top, and the child has to compare the figure on the top with one of the six figures on the bottom and make the correct choice.

Two measurements are made. One is the latency of response, how long the child deliberates before making the choice; and secondly, how many choices he makes before he makes the right choice. If you are still thinking then you are reflective types. If you have decided already, you are relatively impulsive.

But this is the right choice I think. [Laughter.]

Let us go back to the next slide, the first slide. The field dependence-independence test is a test that has been around for some time. It is a measure of foreground, background discrimination. It has been standardized by Witkin. Dr. Keogh has been quite interested in this test for a number of years, believes that it is one of the most useful measures around for looking at attentional behavior in children with learning disabilities.

We have been using this test, and I will show a slide from that test in a moment. The third test is a measure that is now called the children's checking test, developed by Judy Margolis. It is essentially a vigilance test, and the way it works is that a tape recorder delivers a sequence of numerals to a child who is sitting at a desk with columns of figures in front of him, and the figures delivered from the tape recorder are matched with the columns of figures in front of the child. Periodically there is a discrepancy between the figure that comes out of the tape recorder and the rows of figures in front of the child that he is following with a pencil, and he has to make a cross when a discrepancy occurs. It is a sensitive way of looking at a child's vigilance ability.

We have been most interested in this task for a number of reasons. One is that it seems very sensitive to the hyperatcive state, and secondly, we worry least about practice effects because there are a number of alternate forms available, and Judy Margolis has shown that there is very little practice effect after the first few minutes of the task. The task has to be carried out for 20 minutes. It is an incredibly boring task in some ways, and in many ways is an excellent mimic of some aspects of classroom behavior.

So it does test the child's ability to attend to things that have relatively little intrinsic interest to him.

Then finally the Porteus Maze is a test that has been around a long time, and tests the child's ability to trace, to get—what is the expression I am looking for? To track through a maze with a pencil, and it has a certain motor load to it, and has been shown to be sensitve to some extent by Dr. Conners as well as others to the presence of hyperactivity, and exhibit effects of—and change when stimulant drugs are administered.

Another reason we are interested in this battery is, there are all pencil and paper tasks, with the exception you need a tape recorder for the children's checking tasks. We liked this idea because we feel that it at least has the potential of widespread use, should these tasks be shown to be of value in the clinical management of hyperactive children, rather than highly instrumentated kinds of evaluations that can be carried out in one or two laboratories but cannot get much beyond that, and certainly cannot be used in the physician's office.

We would like at least to have the possibility, if not a physician, at least a clinical psychologist or a psychometrist, a person who does testing in a clinical way, to have the opportunity to use some of these measures.

Let us go on to the next slide, please. This is a sample from the children's imbedded figures test, the Witkin task. The top is the simple figure, and the child has to recognize or disimbed the simple figure from this complex figure here. There should be a line over here, but it did not come through this slide very well, but this is where the simple figure is.

This test is scored on the basis of an initial correct or incorrect response.

We are somewhat worried about the question of practice effects in some of these other measures. There are alternate forms of the match familiar figures test, and we are presently looking at our data to see just to what extent the practice effect is a problem to us.

Now, I think we can have the lights, please.

As I said, we are not too worried about the placebo effect. One reason I am not too worried is that in the studies that we have carried out, and a previous study that we have completed and published, we found very little placebo effects with the use of methylphenidate. In a group of 48 children under double blind conditions, we only found 1 of 48 where we got what we regarded as a significant response to a placebo agent.

I am aware that the literature has a lot of data about 20-, 30-, 40-percent placebo responses when interventions, therapeutic interventions, are applied to hyperactive children. I think that one of the main reasons for our lack of placebo effect is the kind of patients we see. We are in a pediatric clinic, and in fact, children who come from seriously disturbed families, dysfunctional families, who exhibit serious secondary behavior disorders or conduct disorders of their own are excluded from our study.

Some of this represents my own personal feeling that drug interventions, anyway, I do not think I would feel this way about dietary interventions, but drug interventions should not be carried out in children who come from seriously disturbed families or who themselves are exhibiting significant conduct disorders.

We have children who have relatively pure hyperactivity syndromes if there is such a thing. But what I mean by that is that their problem is mainly in the domain of attention. They are impulsive, distractable, restless, short attention spans, but otherwise they tend not to have serious behavioral disturbances.

I think that those are the main remarks that I would like to make. I will stop here now.

Dr. Kolbye. Questions or comments directed to Dr. Schain?

Dr. Lipman. Which causes them to flush, is that niacin or niacin amide?

And have you tried this dose with this type of children before and are you somewhat concerned about a high dose response with the children of this type?

Dr. Schain. I am not aware of this phenomenon.

Dr. Lipman. There is, with either niacin or niacin amide.

Speaker. Nicotinic acid.

Dr. Margan. I would like to pursue that question a little further, because I would like to just bring up the question of, again, I thought your original proposal really sounded better to me than introducing 20 milligrams of nicotinamide, even though it is supposedly an innocuous compound. We all are dealing with innocuous compounds. This is a compound—they are all supposed to be innocuous.

But we really do not know. And I would say even with nicotinamide, we do not know why introduce it. I mean, you might be doing the adverse—you just might be introducing an adverse agent along the way.

I would certainly suggest that if you are going to use something, use something which would have no effect.

Dr. Schain. I am very sympathetic to that feeling, but I do believe, and I have grown to believe even more strongly, that making a nutritional intervention has a substantial impact on the family, on the parents, on the parents' perception of the child, et cetera, et cetera, et cetera.

Dr. Margan. I agree 100 percent.

Dr. Schain. So I am really open to other kinds of nutritional intervention, but I think that we should do something, and I do not think we can really deceive parents totally and tell them that a placebo is a nutritional intervention.

I do not think that is right.

Dr. Margan. I agree with you. But unless one is to explain the very nature of this, there will be——

Dr. Schain. Well, then——

experiment, you cannot do so.

Dr. Margan [continuing]. But obviously in the way you have designed your experiment, you cannot do so.

Dr. Schain. To get parents to agree to a 6-week placebo intervention with their children, in whom they are greatly worried, greatly disturbed, who are having school problems, and who are entering into a research project with some hesitation in the first place, is really very difficult.

Dr. Margan. Well, I would suggest in place of that the preparation of a very excellent total vitamin preparation, which you cannot buy on the market today anyway. Maybe have one of these prepared——

Dr. Schain. That may be a better idea.

Dr. Margan. Give a total vitamin, let us say mineral, trace mineral mix, which assures your child of having at least adequate nutrition in this area, which you cannot get out otherwise.

Dr. Schain. That is a little better than a placebo, is it not?

Dr. Kolbye. Dr. Lipman, did you have another question?

Dr. Lipman. No; I am just agreeing.

Dr. Kolbye. OK. Any other questions?

Thank you, Dr. Schain. Now, we are set up for coffee, and we will take about a 6-minute break and then we will hear from Dr. Feingold's group.

[Brief recess.]

Dr. Kolbye. Dr. Weiss is going to speak for the next research group, which includes Dr. Feingold. After Dr. Weiss is through with his presentation, I would like to invite Dr. Feingold, if he wishes, to make any comments or suggestions to the group to please join.

Dr. Weiss?

Dr. Weiss. I am a behavioral toxicologist and pharmacologist, so it comes as no surprise to me that there are chemicals that influence behavior in the nervous system. For that reason, I did not dismiss the Feingold hypothesis out of hand when Ben called me one day to ask about Russian work in this field.

We also know that there are many food intolerances, some of which are expressed as central nervous system effects, many of them vague, subjective complaints, like irritability, headaches, fatigue. I suppose all the components of what psychiatrists used to call the neurasthenic syndrome, and many others.

As a behavioral pharmacologist, I am a little disturbed by the emphasis in the planned research that I have heard reported today on the syndrome of hyperkinesis. It seems to me that if the possibility exists that certain elements of the diet exert behavioral effects, that one single syndrome will not reflect the total potential they have for changing behavior.

Hyperkinesis as seen in the affected children is a very dramatic syndrome. But there are many other ways in which chemicals act on behavior.

The hyperkinetic syndrome may only reflect one kind of predisposition to respond. Other behaviors may be just as important. For example, take amphetamines, which in a number of studies has been shown to significantly alter hyperkinetic symptomatology. We know from many basic studies in behavioral pharmacology that the action of amphetamines and other drugs depend on the baseline behavior, that in certain circumstances, these so-called stimulants, a term that we have tended to drop, may depress behavior.

For that reason, I would not disregard a protocol which also assesses the possibility for alterations in behavior other than increase in activity.

Now, our own interest, Dr. Margan's and mine, in this problem, was strengthened by a visit we had paid to the Santa Clara Kaiser Permanente Medical Center. The Department of Pediatrics, under the chairmanship of Hicks(?) Williams informed us that they had something like 26 families who were adhering to the Feingold diet. Adhering because they had noticed significant changes in the behavior of the children.

They made their records available to us, and also discussed with us on an anecdotal level some of their observations. They were aware that nothing firm had been established because of the absence of the conditions that we impose for a controlled clinical trial, but they were more than willing to assist in what we considered to be a more critical evaluation of the hypothesis.

After looking over the records, and talking to these pediatricians about the affected children and their families, we came to the conclusion that perhaps the best approach would be to use these families who, at this point, have been adhering to the diet for a period of at least 5 months, and to concentrate on the youngest children, because there you have the most limited kinds of diet, the most limited access to other dietary constituents, and the most limited social behavior.

At the present time there are 12 children between the ages of 1 and 3 in the families that are adhering to the diet. What we would propose to do would be to study these children in the following way. In a 60 day trial following the baseline period, we would challenge them on the average of once every 4 days with a randomized design a formula made up in the Department of Nutritional Sciences at Berkeley under Sheldon Margan's direction.

On the treatment days we would provide for them a combination of 3 azo dyes, amaranth, sunset yellow, and tartrazine at dose levels equivalent to the ADI recommendations of WHO.

That means that, within a 60-day period, we would have 12 challenges, each preceded by at least 3 control days, 2 control days.

Parents would make daily reports to a research assistant on a variety of symptoms that from the clinical impressions seem to embody irritability, crying episodes, tantrum behavior, and say, sleeplessness.

These seem to be four characteristic responses that the parents in this population have reported as being modified by adherence to the diet.

There are lots of details that I will not examine at this time. Those of you on the committee can see it in the proposal.

In addition, we would like to develop, with the assistance of the Kaiser Center in Santa Clara and elsewhere, a population of infants. That is, children below the age of 1, who are maintained on formula and who seem to show an aberrant response to vitamin drops. These are universally prescribed by pediatricians and, in a number of instances, have been pointed to by parents or pediatricians as the instigating agent for episodes of colic, crying, et cetera.

These are all disturbances that a parent finds relatively easy to discriminate in contrast to some of the problems that arise with older children whose behavior may in large measure be under the control of peers or their social environment.

You can see our strategy. We are trying to refine a situation into its simplest components so that we can develop a design that mimics the most effective clinical trial designs that are used for the evaluation of drugs.

In that case, the challenge agent would be the synthetic flavors and synthetic colors in the vitamin drop preparations.

I have given you only a relatively brief description of the details, as I said before. I would be glad for the next few minutes to answer any questions.

Dr. **Boesel.** Why challenge the children in the first study only with dyes, rather than flavors?

Dr. **Weiss.** The question is, Why challenge only with dyes rather than flavors? The answer is, Simplicity and clarity of design. Let me finish my answer, please.

There are several instances in the literature where intolerance to colors have been reported in adults. I will take tartrazine as an example. There already is documentation therefore that some predisposition to respond aberrantly to these colors exists, and for that reason we thought we would simplify matters and use those which I think are the most commonly used coloring preparations.

Dr. **Hersh.** I had a number of questions. I may have missed this in your presentation. One was about the question of controls. Given the age, there are many questions about controls, but particularly in the context of the ages that you are dealing with, a group of 1 to 3 and also less than 3, in the developmental phenomenon that children change very rapidly, and the kinds of things that you are looking for, and also that this is an age where the physical contact with the parents is very intense, and can be, when there are special procedures and things introduced, enhanced—it would seem like you just would have to have some kind of control. Or you would not know what you were getting at all.

Dr. **Weiss.** That is the reason we are using a double blind—not that the children have to be told anything—crossover blind. That is, a formula is prepared for each of the, say, 70 days, 10 baseline, roughly, and 60 experimental days; on a prescribed time at each day, say at 12 noon, the child gets a formulation. Each bottle or custard jar is labeled, 1, 2, 3, 4, 5, or with the date.

On certain days, the formulation will contain the combination of colors. On other days, an equivalent preparation without the colors, but looking and smelling and tasting exactly the same will be administered by the parent.

The question of controls always arises. The best we can do under these circumstances is to use the correlated control, which is the child itself.

Dr. **Hersh.** And what about the question of—I know you address yourselves to human experimentation, and one of your comments there in toxic effects is that test agents are commonly found in prepared foods. Are they, in this amount, are they ingested by 1- to 3-year-olds, or by less than 1-year-olds?

Dr. **Weiss.** I do not know what the amounts are, and I do not think anybody else does, because the food manufacturers will not give us that information.

I do not think anyone has a firm notion of the age distribution of intake of any of these constituents. There is another problem as well that I do not think anyone has addressed themselves to. That is the question of chemical transformation and the preparation of foods.

Some of the red colors are not used or have not been used recently in the preparation of candies because the processing makes the colors fade, which indicates that they undergo a chemical transformation, so pigments, like Red No. 2 have been used, to give candies a red color. I would be willing to bet that in processing of candies they undergo some kind of chemical transformation, not to mention the kind of chemical transformation they may undergo while being metabolized.

I think even a test of the colors themselves may not be adequate alone without a test also of the degradation products or the chemical modifications that occur after they are added to foods and the foods are processed.

Speaker. Have you considered the potential carcinogenic effects of the drugs, I mean the dye, whatever they call the food color? For one thing, the younger the child, the more susceptible they are to these, and I think amaranth is one of them.

Dr. **Weiss.** The question is——

Dr. **Kolbye.** Excuse me. As chairman's prerogative, I would like to turn to Mr. Gittes before you respond to that question on the amaranth carcinogenesis.

Dr. **Gittes.** I think the question of carcinogenesis is really, in my view, for these colors that are used in food testing, they just are not carcinogens. We have extensive animal testing which says they are not. If they were carcinogens they would not be permitted.

Red No. 2, as well as tartrazine and the other food colors have been tested in animals quite extensively.

Dr. KOLBYE. This is an informational point. Dr. Weiss?

Dr. WEISS. I guess that is sufficient response to the question of carcinogenesis.

Dr. KOLBYE. OK.

Dr. CINQUE. You are proposing to ask the parents to rate factors such as irritability, crying episodes, excessive motor activities and sleeplessness, right? And the scale you intend to use on this is the scale you include in this proposal?

Dr. WEISS. Yes.

Dr. CINQUE. I presume that this scale has not been standardized or used before?

Dr. WEISS. No; it has not been standardized or used before.

Dr. CINQUE. One of the problems I see with it is that it relies heavily on the parents' experience. For instance, it rates according to "less than typical, typical, more than typical."

Dr. WEISS. Absolutely, yes.

Dr. CINQUE. But that would be a highly subjective rating on behalf of the parents.

Dr. WEISS. Oh, but the parent has no absolute scale unless the parent is trained to sit down and say, take time samples, and is trained as a behavioral observer. Now parents can be trained to make behavioral observations of that kind. That would be desirable. But to maintain this population for this period of time, I thought it would be optimal to use the simplest kind of behavioral descriptions available.

Parents do have an implicit scale based on their own experience. It is the kind of thing you see in all kinds of psychophysical studies anyway.

Dr. CINQUE. I think that is my point, that the experience would vary from one parent to the other.

Dr. WEISS. That is right. We cannot build in an absolute scale and have a relatively simple experiment. If you go into the literature on analgesics, for example, which I think you will find enormously consistent, then you see that patients can do very well at rating whether or not they have severe pain, moderate pain, mild pain, et cetera, and that you get extremely consistent dose response curves with opiate analgesics.

It is a kind of psychophysical study. We have no control over the stimuli but in the same way that an observer in an experiement on vision can respond by saying "yes" or "no" to the detection of a target, we are having parents make the same rating. You cannot get inside the observer's head, but he does have a scale. And there is a large literature on scaling anyway in psychophysics that I cannot discuss here anyway.

Dr. CINQUE. One other point. I think it has been suggested by Sprague that the hyperkinetic child does most poorly in a structured situation, such as the classroom situation. Obviously, this population would not lend itself to testing in that situation.

Dr. WEISS. That is right. We made a deliberate choice of the youngest children thta we could obtain in order to find children who remained at home in the relatively uniform environment, under the control of one or two observers, who have this implict scale and experience, and who have limited dietary access, and a limited social environment.

Dr. SILBERGELD. I am very attracted to the simplicity of this, and I think I just have two questions which might add information to it. You seem to be relying on the background to this question, which has a great deal to do with allergenic effects of some of these compounds.

Are you going to look at the immunologic status of these kids at all? It might add some interesting information.

The second question would be based on what was mentioned in several studies and here too, which is in rapidly developing young children, would it add anything, do you think, to have a cohort study, perhaps even children that did not come under the original Kaiser-Permanente study, just carried through and being rated by their parents, just to see what the normal fluctuation in ratings might be on a subjective scale.

Dr. WEISS. Let me respond to the second question first. Yes, it would be desirable, but I think for a preliminary study which we regard this as being, we would like to concentrate on a small population, and get it done as quickly as possible.

As to the first question about allergenicity, perhaps I should let Dr. Feingold discuss this, but we are not really talking about an immunological response. We are talking about intolerance.

And there is——

Dr. Silbergeld. I just thought it would add some information. See, if you did—whatever results you got, since you do have this group, and presumably there would be people willing to provide the clinical services needed, it might be very interesting to get that information at the same time.

Dr. Weiss. You mean to do an allergy survey?

Dr. Silbergeld. Well, to take samples to see whether the—not cocktails—whether the milkshakes that you are giving to these kids are producing, precipitating some kind of chemical response that makes them different as well. It is just an added bit of information.

Dr. Weiss. I think the likelihood of that would be very small, but I would like to have them respond to that, because we have discussed this many times.

Dr. Forbes. Maybe Dr. Margan is the one to answer this question. If you are going to use the dyes in your experimental formulas, how are you going to be sure that they are indistinguishable one from the other from an appearance point of view, because if you are using a significant quantity of dye, it is obviously going to change color.

Dr. Margan. This is the thing which has given me probably the most headaches of all in the protocol, namely, the preparation of a formula which would be indistinguishable from the control and experimental formula.

I have not really played around with this yet, but we have had, as you know, years of experience with this type of thing, since we have had to do this on many occasions. We have not worked much with dyes. But I do believe it is possible to do so.

We will probably have to introduce some type of coloring matter, there is no question at all, into the other material. There will obviously be something else. What it will be at this point in time I do not know. It may turn out to be some type of a brown material, probably caramelized sugar. It might turn out to be a matter of some natural dyes, in which we would have to extract beet juice, for one thing: I do not know what we would get from the red plums, or something. God knows what can happen to the pH.

We think is something that can be overcome. But it is a very critical part of the experiment; we realize that.

Dr. Kolbye. As a suggestion, and I do not know whether it is meaningful, you might be able to take a natural food color and mask the other colors, to a certain degree.

I am sorry for the noise, but it is a choice between air and noise, and we have to breathe.

Dr. Springer. I would like to ask a question about the design. Each time you give treatment to these families, it will be the dye, and that will be given for 1 day?

Dr. Weiss. One day.

Dr. Springer. And then followed by 3, 4, and 5 control days?

Dr. Weiss. Yes.

Dr. Springer. And the parents make a rating on each?

Dr. Weiss. Yes.

Dr. Springer. Do you expect to see the effects of this, * * *?

Dr. Weiss. Did everybody hear that question? It had to do with I suppose the latency and duration of the response on the treatment day. We were guided by the clinical reports from the pediatric staff at Santa Clara. Roughly what we gleaned from them and from Dr. Feingold is that there seems to be a more acute response on the part of the younger children. That is, the latency to onset is shorter, and the duration of effect is shorter.

Now, there are variabilities as pointed out here. There are some children who seem to respond with a very sharp peak, a very quick onset, and a quick decline; others who respond with a sharp onset and a relatively slow decline; others who respond with a relatively slow onset. So the kinetics of the behavior change you might say appear to vary.

We will try, if we have a larger sample than available now to choose what appear to be the most acute responders. But given what seems to be the experience of the staff down at Santa Clara, I think a period of 1 day for the observations—let me put it this way—a period of 3 days following the administration of the agent would seem to be adequate, both to observe an effect, if there is one, and to allow enough time for washout.

Dr. Katz. You talked about kinetics of behavior, and I was goinng to ask you what you knew about kinetics, pharmacokinetics of the dye.

Dr. Weiss. I have no idea of the pharmacokinetics. I am not sure that these have been followed very closely in humans.

Dr. Katz. But it would be very important?

Dr. Weiss. That is right. We——

Dr. Kolbye. Dr. Lipman?

Dr. Lipman. One comment on the design. I think this is the only design I have heard which would actually enable you to say whether a particular child showed a drug effect or a diet effect, in that it is an intensive multiple crossover, and you do statistics with any particular individual.

What I missed though was, How do the families originally get on the Feingold diet, and do you know the children, the 12 children, are indeed allergic, or are you assuming they are allergic?

Dr. Weiss. The question was, How did the families originally come to adopt the diet, and how do we know the children are allergic. Again, we are not, to answer your second question first, we are not talking about allergies. We are talking about hypersensitivity to a food constituent or an intolerance.

How the families came to adopt the diet varies one from the other. They are part of the Kaiser Permanente system in the Santa Clara area. They came to the attention of the pediatrics staff with various complaints of the kind that I noted on that rough scale. They were asked to try the diet.

Dr. Lipman. So it was—12 children * * *?

Dr. Weiss. No; there are 26 families on the diet. I think the age ranges of the children are from about 9 months to 13, 14 years.

We talked to one of Dr. Williams' research assistants just yesterday, and found out that there are now still 26 families on the diet. The minimum time has been 5 months. There are 12 children between the ages of 1 and 3 in this group, and two children below the age of 1.

Dr. Hersh. Point of clarification. These are children who are——

Dr. Weiss. These are alleged responders.

Dr. Hersh. Alleged responders. Oh, OK.

Dr. Weiss. It is not a random sample of children. Or even a random sample of so-called hyperkinetic children.

Dr. Chopra. I would like to find out, what was the earliest age you have been able to diagnose hyperkinesis.

Dr. Weiss. The question is the earliest age at which we have been able to diagnose hyperkinesis. We are not talking about hyperkinesis. We are talking about behavioral disturbances. These are manifested in the very youngest children, in the infants, as episodes of sleeplessness, excessive crying, colickyness.

Dr. Chopra. But these could be attributed to allergy due to milk or anything else.

Dr. Weiss. That is right. They could be anything.

Dr. Chopra. Right.

Dr. Weiss. That is right. And that is why we want to make a test on these children, whose behavioral repertoire and behavioral environment is very limited, of three major colors that have been implicated.

Dr. Symmes. The study you have proposed approaches but does not quite reach the ideal. It is the best possible population; the agent is identified and focused upon. But I am critically concerned at the lack of an objective measure. This is not just a general worry, but my awareness that humans and animals can discriminate drug effects without knowing what they are.

I refer, for example, to the work of Herbert Waring, in Pittsburgh. There is therefore the possibility that either the children or their parents will see a change which they cannot correctly identify or describe, and they may report to you anything, including that the diet makes them sickly, or the diet makes them very active, or the diet makes them feel gay. And it really is critical——

Dr. Weiss. You are using gay in the old sense, I take it? [Laughter.]

We will attempt to arrange a study in which the parents are contacted every day. We have made room on the form for any unusual responses that we have not included in the categories here, and as well we plan to carefully instruct the parents in what these categories encompass.

Now, by objective measures, I assume you mean getting something like frequency counts of certain items of behavior. We will have——

Dr. Symmes. We have had much testimony this morning about different objective measures.

Dr. Weiss. That is right.

Dr. Symmes. I am not suggesting one in particular, but that——

Dr. **Weiss.** Yes; as much as possible we are going to have research assistants visit each of the homes on two or more occasions, at which point they will be taking observations of the child. On at least one of these occasions, the child will have been administered an active agent for the treatment. On another occasion it will have gotten the control preparation.

The problem I think arises in having enough people sitting around getting so-called objective measurements. I do not think for a study of this type it really makes sense to develop a large enough staff to do that.

We first want to find out if there is anything to be seen with a challenge of this kind. For such a purpose, I think educated parents; that is, educated by our staff, can serve an appropriate discriminant function. That is, they can tell whether or not the child has kept them up at night, or whether the child seems to be more irritable on a certain day than on another day. I can certainly tell with my kids whether or not they are more irritable or more depressed than they typically are.

Dr. **Kolbye.** Mr. Margan, do you have any comment?

Dr. **Margan.** Yes; I am not certain whether I understood your question right. I understood you to ask a slightly different question, in that you asked the question in the context that many drugs have certain nonspecific effects, and what might then be noted is a secondary effect, which you might interpret as a behavioral effect; is that correct?

Therefore we would be looking at the wrong things. Now my concern would be just as great if the behavioral effect were "secondary" to some other effect. I would not know which was primary or secondary, you know, in either instance. And as Bernie points out, that is why I feel it is so important that not only do the parents rate these four scales, but they do report, as you have suggested, anything else that they might observe which, to them, is some form of aberrant behavior on the part of their own child.

Dr. **Wender.** It seems to me that there is an important issue that is being overlooked here. One is that there are two factors to be studied on this whole question. One is seeking the truth of whether there really is something in colors and additives that is harmful to people; and the second is the hypothesis as stated by Dr. Feingold that hyperactivity, which we know is a large and a common problem, and has achieved a great deal of publicity, is a condition which indeed is adversely affected or perhaps even caused, as has been claimed in some instances, by the presence of these items in the food.

Now, it seems to me this study is very well and good, but unless you have some connection between the behavior of these kids and the subsequent hyperactive behavior syndrome, then whatever it is you are establishing with this study will have absolutely no applicability to the other question that has to be answered.

Now, the behaviors that you are looking at in these kids are behaviors that have been reported by some people as antecedents of hyperactive behavior, but we do not know that that is true. Until we have some objective data about these particular behaviors in infancy, and following them longitudinally we will not know the answer to that question. So it seems to me you are answering an interesting question, but it is not the question we need answer.

Dr. **Weiss.** I think your priorities are reversed. Because the main question to ask is whether or not these substances have any kind of discernible physiological or behavioral effect. And if they do, then a lot of important issues have been raised that go way beyond the question of hyperactivity or hyperkinesis or any specific syndrome of psychological complaints.

Dr. **Wender.** Yes; but it depends upon a discernible effect on what size population and in what conditions. Obviously the social applications of the effects of these things depends upon the size of the population that you are dealing with, into that particular population are very important.

I mean, we know some people are sensitive to aspirin, but that happens to be a fairly small number. There has not been a sensitivity which has caused us to be concerned about eliminating aspirin from the pharmacopeia. I mean, the questions about the population that it affects or the number of people that fit into that particular population are very important.

Dr. **Weiss.** Of course; that comes later. Ellen?

Dr. **Silbergeld.** Why can't you run—it seems to me that what this is growing out of is a very real concern with simplifying the outcome measures and the population.

I like the idea of taking a population that is an established responding group, and a group that has pretty well defined characteristics.

Why don't you do an animal study?

Dr. KOLBYE. I would like to turn to Dr. Kerr.

Dr. KERR. In the same area of Dr. Wender's concerns, Dr. Silbergeld said it was important to work with an established population. I cannot think of any population that is less established than children of this age. How do you quatify excessive crying? Excessive crying is something that is a two-way street. Somebody has to hear the crying and respond to it.

You say that at times you are more sensitive, or you appreciate that your children are different than they are on other days. Perhaps some of that difference is in your powers of observation on those particular days.

I really think this is a most difficult area. We know so little about behavior of children in this age. We do not know why they act the way they do on certain days. We have no appreciation of what colic is, except it is a rugged thing when it develops, and I think really there has to be some way of quantifying objectively what these measures are. And to say he cried excessively on this day I think really does not get to where you want.

Dr. WEISS. Look—this is not the critical ultimate study. If I were designing that, it would be a hell of a lot larger and cost a hell of a lot more and take a hell of a lot more time. We are looking for whether or not there are preliminary indications that these substances do in fact produce behavioral disturbances.

Now, if you go into the literature of applied behavior analysis, you will find that parents can be trained to be fairly good observers of their children's behavior, and in fact can be trained to become talented behavioral engineers and do behavior modification with children.

So I have no doubt that this group of parents can at least be trained to make reports about whether or not the child's behavior on any particular day is typical of that child.

Dr. KOLBYE. Dr. Lipman?

I am sorry to interrupt you; did you have a question or comment earlier?

Dr. LIPMAN. On the question of other kinds of measures, it seems to me very easy. People have used actometers on kids. Bob Sprague has a measure which I am sure could be modified for the crib. You know, the kid is young enough—to get some measure of, you know, threshing about, and that kind of thing. I do not think it would be very difficult. It is not, you know, it is not that much of a problem I would think.

Dr. WEISS. There is no such thing as such—a study. I have never encountered any such species. And the more complications you add, the more difficult it is to carry out the study, the more difficult it is to get reliable observations in the home, and the longer it is going to take.

I do not do this kind of study routinely. My laboratory has four computers in it, and that is the way we like to do behavioral studies. It is impossible in this situation to carry on that kind of experiment.

Dr. KOLBYE. Dr. Weiss, I think you have stated your points well. I would like to ask Dr. Feingold, since you have had the first word on many things, would you like the last word? Would you like to wait until after Dr. Lipton makes his presentation, or would you like to comment now?

Dr. FEINGOLD. Whatever your pleasure is.

Dr. KOLBYE. Be our guest.

Dr. FEINGOLD. I had not intended to elaborate on Dr. Weiss' presentation. But I think it would be important to clarify a few points, particularly the one raised by Dr. Silbergeld relative to allergy, and secondly I think the question repeatedly raised by Dr. Wender relative to solicylates.

I think I mentioned on several occasions, those of you who have heard me speak, that it is rather unfortunate that the historical development of this whole hypothesis is first identified with myself, who am an allergist and an immunologist, with the result that everyone feels this is allergy, and in spite of the fact that I repeatedly emphasize that this is not an allergic mechanism. I constantly hear that brought up.

I will elaborate on that further.

The same thing applies to the problem of solicylates. The historical diet involved our experience with aspirin and cross reaction with tartrazine and all the other compounds, and because of that the emphasis is constantly on salicylates which is a minor part of this problem.

I have learned that now, much to my regret, over the years, it is so confusing to everyone that for larger scale programs I am recommending that they start with part II of my diet, just colors and flavors, and omit the other, and then work backwards. All it will do is reduce the incidence and frequency of responses.

Now, to get back to the allergic component. I believe it is pretty well recognized, and as a matter of fact I think there was a recent study by Howard Johnson of the FDA at the Cincinnati Immunological Laboratories, whether or not these compounds behave as heptanes. He came up and said "It is not a heptanic mechanism."

You see, these low molecular compounds to have an immunological response must act as heptanes and conjugate with the protein carrier to give it immunogenicity. We know the behavior of heptanes. Very rarely, I do not know of anybody who has been able to demonstrate an I.G.E. antibody mechanism involved with this.

If we seen an immunologic response, we were to see an immunologic response, it would have to fall into the other categories, of either the intermediate, like the arthus type, the delayed hypersensitivity, or the cytotoxic.

I know of only one report on an adverse reaction associated with tartrazine where they were implicating this and suggest an allergic mechanism, and that is a thrombocytopenic purpura as reported by Crape of Pittsburgh, where they think it might be the cytotoxic effects.

Now, where we are dealing with a heptanic mechanism, in all the years we have been following these, not only in behavior. we have been following these compounds clinically for many years. We never see maculopapular rash. We never see any of the evidences as I suggested of those mechanisms. And then when we come to aspirin, we see, that in dealing with aspirin, which is closely allied in cross reactivity, the consensus is that it is not an immunologic response.

Now, what is that response? In aspirin to date we have two mechanisms that have been demonstrated. First, we have the acetylation of the epsilon aminoradical of lysine, by virtue of which we have involvement of the lysino-collagen, the lysine in the platelets, and the lysine in the albumin. So when the albumin interferes in the carrier mechanism; in the collagen, it interferes with the activation of the Hageman factor, leading to bleeding. And in the platelets it interferes with the aggregation, also to bleeding.

We do not see bleeding here. Now, the second mechanism. The second mechanism has to do with the inhibition of PGE-2 prostaglandin. That work was so very well done by Vane and Farrar in London.

Now, thinking that there might be some relationship there with the cross reactivity with tartrazine, I supplied Farrar with two samples of tartrazine. There is another point I want to make. And he repeated his studies on animals with two samples of tartrazine, but was unable to duplicate it. He could not demonstrate inhibition of tartrazine—PGE-2. But he told me that we would have to look at the metabolites. There may still be something there that we do not know, but it is not immunologic.

Now, as far as cross reactivity, when I am talking about tartrazine, I think it is important to bear this in mind. There is unquestionably cross reactivity between tartrazine, aspirin, and the other dyes, too.

What the incidence is we do not know. But, for instance, Samter and Beers report the 7.5 percent cross reactivity between aspirin and tartrazine. There is a very recent report, if you saw the Journal of Immunology, this current issue. There is a work by Sutterpane out at Rhode Island, who has been interested in this problem for years. He feels there is about a 15 percent cross reactivity.

Now, what is the importance of that? If there is 15 percent cross reactivity with aspirin, and you omit the solicylate from the diet, the most you are going to have is reduced by 15 percent, but you are still not going to cut it out completely.

So if you are going to complicate everybody's life, I say, drop it now until you go ahead.

That is the immunologics. Because the solicylates are not the important thing at all.

Now, there is one other thing you have to bear in mind. We have two mechanisms that have been demonstrated for aspirin. But that does not mean those are all the mechanisms, because neither of those mechanisms fit in with the problem we are dealing with now. I have talked with pharmocologists, particularly Farrar, who has worked with that. I have also talked with Freiss right here in town. There must be some other mechanism. We have not uncovered that yet. It is going to take many years.

Now, Ernest Freiss suggests it is conceivable that there may be specific binding sites or receptor sites on the cell walls, specific to the compound, so although they are not identical structurally, they still produce the same end results.

But we have to look at that.

I had not intended to go into any of this, but the question came up, and I think it is important to clarify it.

I did rather intend to make some general comments.

Dr. KOLBYE. I wonder if I could ask, Dr. Feingold, on those, if you could hold for about 20 minutes, until we have Dr. Lipton's presentation.

Dr. FEINGOLD. Fine. You want me to make them later?

Dr. KOLBYE. And then we would like to hear from you.

Dr. FEINGOLD. Fine. Thank you.

Dr. WEISS. In the budget, there is per diem listed for me for 4 weeks at $4,000. It is $14.

Dr. KOLBYE. OK. Dr. Lipton?

The question was asked, $14,000? [Laughter.]

Dr. Lipton, thank you for coming.

Dr. LIPTON. Thank you. I am sorry I got here late, and I have not heard the morning papers. I did though hear Dr. Weiss', and some of the others. I do not have data to present, nor do I have a well defined protocol. I suppose really I would have liked to have had the ultimate word, but I will settle for the penultimate word.

I should begin, I guess, by saying that I am delighted that you are having this meeting. I got into this business myself interestingly when called upon by the Nutrition Foundation to chair a task force or a group to examine the data. I think the reason that I was called was that I had had a similar task given to me by the American Psychiatric Association in relation to the problems of megavitamin therapy. Some reference was made to this earlier.

I hope that this issue does not, in a sense, degenerate into what has happened with megavitamins, which after almost 10 years are still fulminating as an unresolved question, with strong, loud opinions on both sides, and with very little experimental data, particularly by the advocates, I might say.

It is for that reason that I am delightful, and I am also delighted that Dr. Feingold and Dr. Weiss have started experiments, that I would hope would permit a reasonable resolution of this question within a matter of 6 months or a couple of years or something of that sort. I think that it can be done this way.

Now, I think I prefer what might be called the experiment which is as sloppy as possible. I say that to be interpreted literally, meaning no more sloppy than possible, and not necessarily less sloppy than possible.

It is for this reason that I think that issues, for example, like animal models are secondary; issues like the mechanism of action are secondary. The primary question really is, does one have a phenomenon, and a phenomenon which can be clearly demonstrated.

The issue if hyperkinesis is a troublesome one. If we accept Dr. Feingold's estimates, he gets about 50 percent response, somewhere between 30 and 50 percent response to the K-P diet, in hyperkinetic kids.

That should permit a rather large cohort that one should be able to get. I find myself somewhat disappointed at the fact that the cohorts get small repeatedly. I had hoped, for example, that Dr. Feingold had several hundred kids that were on the diet, and that one might be able to get that cohort, and that would be a very important cohort, because these are children that have responded.

Apparently now we are down to 26 families, and I would wonder, for one thing, what has happened to the others. Have they outgrown it, or in some way become dissatisfied with it, or what?

I also want to make the point that while I thoroughly approve of the 1- to 3-year-old study, because that makes compliance easy, and makes the behavior fairly simple, I would also agree with Dr. Wender that the issue is hyperkinesis, and I certainly do not see any incompatibility between doing the 1- to 3-year-old study and simultaneously doing the other study. Both should be done, and it seems to me both can be done.

Now, there are various ways in which the problem can be approached. The Wisconsin group has one approach; Keith Conners has another approach. We have debating in North Carolina to use still a third approach. But I do think that the quickest and easiest answer can come from using Dr. Feingold's cohort, getting his participation in these responsive children, and then doing the appropriate double blind study.

Dr. Weiss says they are working with three dyes. I am informed by the Nutrition Foundation that there is now available a brownie or a chocolate bar, and I understand the chocolate is permitted, but the brownie or chocolate bar with or without eight additives, additives in the dose that would be estimated or has been estimated that the average kid who is taking Tang or a variety of other things would take.

The chocolate is a very effective masking agent. I have seen some of the cookies. I cannot tell them apart. I think one would have to chromatograph them to tell them apart. So there would be, I think, effective double blind.

Now, around this I think one can design an experiment, whether it is done on a three schedule or whether it is done on a three-times-a-day schedule, can be worked out.

I do think that the population of kids that were initially studied, which I presume were kids in school, meaning school age then, should be examined as part of this group, and again with ratings by teachers, by parents, and if possible by independent observers.

I cannot see any real difficulties in doing this kind of experiment. I think it ought to be very straightforward, and I think it should be done.

At the same time, I certainly applaud the experiments that are being done by Dr. Wender and Dr. Conners and the Eichman group at Wisconsin, and possibly our own group, and any others that want to get into it, because should the results turn out to be positive, it will certainly represent a subgroup. How big the subgroup will become important. And then of course the whole issue of mechanism and all kinds of implications will be terribly important, and one will have gotten a leg up at least on that through the variety of studies.

That is about all I have to say. I did—I think you have a statement that I had submitted to Senator Kennedy, mailed in after I had seen the statements that had been made by Dr. Feingold at the previous Senate subcommittee. There is nothing in that that I have not said here, and I trust that it would meet with your approval or constructive criticism. Thank you.

Dr. Kolbye. Thank you, Dr. Lipton.

Dr. Weiss. May I make a correction? Those 26 families represent only what is available now through the Department of Pediatrics at Santa Clara. They do not represent all the families all over the country on the diet.

Those are the ones that we know are actively adherent to the diet. They have a selection of 74 they maintain rough contact with. But without anybody standing there are supervising the study, the families tend to evaporate. Peripheral populations evaporate. That is Weiss' law. If you want to get rid of a disease, begin to study it, and then the population dissolves. [Laughter.]

Dr. Cinque. Dr. Feingold, has this population been—when they entered the diet, before they were put on the diet, was it established that they had hyperkinesis? Was any kind of objective rating scale used?

Dr. Feingold. Oh, yes, most of the children were being seen—they were seeing psychiatrists, psychologists, pediatricians. They have been to the medical center. They have had everything you can dream of. Some of the earliest cases were studied for over 2 years.

Dr. Hersh. But the issue is, is there objective rating data establishing the diagnosis?

Dr. Feingold. I have got the information right now on their performance. As we look back over a period of years, now, we have had these for several years, 2, 3 years or so—that is the best index, how does the child perform at school?

Dr. Hersh. I have a question really, it is a question/consultation to Dr. Lipman and Dr. Feingold and anybody else who wants to answer it. My basic question is, I would like your frank response as to whether it is a foolish question or whether it is a useful one, et cetera. About 1½ years ago there was a National Academy of Sciences mission to the People's Republic; I mentioned this in a meeting with Dr. Feingold a number of weeks ago.

Before they went, they were specifically instructed—this was a behavioral scientist—to look for hyperactivity in that country, into hyperkinetic syndrome.

In the places they were allowed to visit, they specifically asked about it, and visited different clinical facilities in schools, and did not see any. It also is a country where they used very minimal amounts of food additives in terms of coloring agents and flavors.

This was reported to me by I think one of our most distinguished scientists at NIH, Marion Yarrow, who is head of our behavioral psychology laboratories.

My question is, given that kind of observation by that kind of group—again, it was a casual observation in the context of, for example, what you just said, Dr. Lipton, while one is trying to fund additional studies, would it be worthwhile to send to that country a particular study group if it is true—or at least try to gather information—is it true that they do not use coloring agents? Is it true that there is not such a thing as hyperkinetic syndrome? Or are the complexities of cross-cultural studies such that it is a foolish question? I am asking it straight out, and maybe it is a foolish question.

Dr. LIPTON. I do not know whether I would embarrass you by saying I agree with you, it is a foolish question. No; I do not really mean that. I do mean that it is very difficult for me to imagine that in any culture there is no hyperkinesis. They may not have noted it, and possibly the incidence is a lot lower than it is here. I just do not know.

But that there is none is just very hard for me to imagine. There may be some on the basis of brain damage; there may be some on the basis of all kinds of other things. So there should be some, and I think you got simply a casual statement, that they said there was none.

SPEAKER. They also do not have mental retardation——

Dr. LIPTON. Yes; and I was reminded that, what was it, in Okinawa some 20 years ago there was supposed to be no schizophrenia. I think one cannot trust these reports terribly much.

I think it would be very interesting—I suspect that if you asked for volunteers, you would get three-quarters of the room. We would all love to go, and do that study, so you will not have any trouble getting observers. But I do not really think that it would add very much, at this point.

Dr. HERSH. What about, we have gotten reports from different places around the world from scientists—we know there are no additives, et cetera, in the terms that we add to our diets, that there is the same level of hyperkinesis—exactly what you said. Is it worthwhile, while one is trying to do the kind of studies that you are suggesting here, to see if some studies can be designed with looking at specific other cultures where they do not use——

Dr. LIPTON. Well, epidemiological approaches or cross-cultural approaches are always useful. It is strategy that has been used in mental retardation and in schizophrenia and in a variety of other illnesses to see whether cultural determinants or viral determinants, or what have you . . . it gives you some clues, but at the moment, I would give that a distinctly lower priority than the testing of a discrete hypothesis which has been made.

Now, if the hypothesis turns out to be correct, it is certainly an advance of monumental proportions. Beyond that, there will still be some hyperkinetics, I presume.

Now, I am not saying it cannot be done. The only thing that bothers is money, and my main comment really is that I think that you are sort of a little in error, if I may use that term, in thinking a study of this sort could be carried out for $50,000.

Dr. LIPTON. Well, my response I think is, first, that Dr. Feingold and I had spoken about this, what, 8, 9, 10 months ago, something of that sort, and we discussed this, and the figure that I give is really the estimate that we had talked about at that time.

Dr. FEINGOLD. Not for 200 children.

Dr. LIPTON. Well, I do not even recall the number. But I am not really concerned with the question of whether it can cost four times that or not. I am fairly sure that it would be cheaper to do it this way than to do it any other way. I think that is well worthwhile.

The other is, I guess, pertinent to Weiss' Law. Where are these families going? When Dr. Feingold talks before the Senate, he talks of millions of kids. And now we have trouble finding a couple of hundred. I think we ought to have another couple of hundred, and to take that, to pick up a subgroup, for example. And I suppose I was in error. I did not know, certainly did not know what the number of kids available was in Santa Clara. I assumed that there were large numbers of children available, which would be one of the great advantages to that study. I said earlier, I am sort of disappointed that there are only 26 families now immediately available. Perhaps it will be too difficult to generate the others.

Dr. WEISS. May I ask a question?

Dr. KOLBYE. Yes, Dr. Weiss.

Dr. WEISS. For any investigator who decides to use that chocolate bar, will the constituents and their dose levels be made available?

Dr. Lipton. I cannot speak for the Nutrition Foundation, but I think so. I think that the wish was to have someone, as I indicated in the latter, someone who is not a part of the research team, by the code keeper.

But he certainly ought to know the code. He should know what is in there; how much; and everything that is—and he ought to be immediately available to the investigators if there is a bad reaction, if—something that requires breaking the code or using an antidote, or whatever there might be.

I do not know myself, you would have to speak to, who it it. Dr. Darby I guess, the head of the Nutrition Foundation.

Dr. Margan. I am curious, Dr. Lipton, as to why they say the—I am just curious from the point of ethics of why they say that the principal investigator should not have the code. If I were the principal investigator, I would in no way utilize the chocolate bar, et cetera, unless I knew darn well exactly what all the ingredients in that material were.

Dr. Kolbye. I think there is a difference between knowing what the ingredients are and knowing which is which.

Dr. Lipton. Yes; does that satisfy you? You want to know the ingredients, not necessarily which candy bar has it?

Dr. Margan. That is right.

Dr. Lipton. I would certainly agree with that.

Dr. Kolbye. Any further questions to address to Dr. Lipton? Dr. Feingold, if you would like to make some additional comments, we have only 5 minutes on the tape. We could take a break and then come back to you.

Dr. Feingold. For another tape, you mean?

Dr. Kolbye. Yes.

We could flip the tape and all take a stretch break.

Dr. Feingold. It might be a good idea because I do not know how long I am going to take. Not very long, but——

Dr. Kolbye. Let us take a quick break right now.

[Brief recess.]

Dr. Kolbye. Let us resume now. Dr. Feingold, would you care to make some comments, please?

Dr. Feingold. Thank you, Dr. Kolybe, for the opportunity to make a second appearance this afternoon. I would like to make just a few general comments relative to the problem.

First, it is very gratifying to experience all this interest and activity this afternoon. I think it is indicative of the process we are going to make. I think it indicates that we are beginning to resolve this problem.

In my various meetings with Dr. Cooper, when I appeared before the Senate committee, with Commissioner Smith, the Interagency Panel, various agencies, I have consistently point out that there are two aspects to this problem. We have first the clinical problem which we must resolve—3 million, 4 million, 5 million—we know there is an epidemic proportion throughout the country.

Second, we have the academic problem. I mentioned my encounters with Dr. Cooper and the Commissioner before here. I consistently pointed out that there are two problems. We have first the clinical problem. That is, managing the millions of children we have. And then we have the academic problem.

Now, this afternoon and all day today, all of you here have been addressing yourself to the academic aspect of research. And understanding and appreciating that these children, like all individuals, have a unique biological profile which makes for a pharmacological individuality. And with the recognition that we are dealing with thousands of compounds, it becomes readily understandable that we are going to have many, many variables on the part of the individuals and on the part of the compound.

That being true, I am certain that many competent scientists and many academicians such as you have done this afternoon will be continuing the debate for many, many years without a resolution, perhaps. More information, but not a resolution of the problem. Because we are a long way from that.

I am the first one to admit that the application of the diet is purely empirical. But as clinicians we have a responsibility to our patients, whether it is empiricism or not, if we are not hurting these children, to treat them with diet.

Now, when I met with Dr. Cooper one of the questions he put to me was, what do I want? I said, "Dr. Cooper, what I would like to have is a statement that there is something there. That is all we are saying. What that something is must be determined over many, many years of costly experiment and many hours of work.

In the meantime, when the parent goes to a physician and consults him for this child, they will not say that dietary management has no value, does not mean anything, and puts him on medication. We are driving these children to medication with drugs. And we have a moral responsibility to see that we do not drive these children to medication.

Now, I know I have had many years of experience with this. I have had many years of experience with the adverse reactions of these compounds that goes back almost 20 years. Behavior is just a new aspect.

I have made observations and others too in the field, and they are reported, and in spite of the fact Dr. Lipton says they are not reported, they are reported. If you ever look at my textbook, I go back and I talk about every one of them individually. And I have other reports.

Now, there is nothing remarkable. If we have compounds here that we can attribute to the adverse reactions affecting every system of the body, practically, is it so remarkable that we are going to have neurological findings? We have never addressed ourselves to that. We never stop to look at them.

Everybody is amazed, because here we are having the behavioral problems attributed to the ingestion of artificial colors and flavors. Any compound perhaps can do that. There is no compound in existence, whether natural or synthetic, that cannot induce an adverse reaction if the individual has the appropriate genetic profile.

We are excluding nothing. But we have to evaluate this on the basis of benefit and risk, and how great the problem is. I feel with colors and flavors it is very great. I feel they are not essential. That is why we have to address ourselves to this.

We have much to do.

I will not belabor the point and go on too long, except I would like to again emphasize the importance of the clinical application of this problem, perhaps empirically. You know from those who have listened to us all day today, there is certainly a suggestion, even in the meager experimentation that has been reported to you that diet does influence behavior. It does not make any difference to the parent whether that is placebo or voodooism or hypnotism or whatever it is. That child is better, does better at school, and is off drugs.

Let all the academicians spend the next decade or two finding out why. In the meantime, we do not have these children sick.

All I am asking you is, do not deny these children an opportunity to try the diet. There is nothing lost. It is not difficult. If they respond, you are a victor. If not, you are no further behind than you were before.

There are many compounds involved.

Thank you.

Dr. Kolbye. Thank you, Dr. Feingold.

This concludes the open session of today's meeting, and I would like to then convene the interagency panel in executive session. Do I hear, going once, any additional comments, questions?

Going twice. Yes, Dr. Symmes?

Dr. Symmes. I think it is so important that the resolution be made; I would address my comment to Dr. Kerr—is there some portion of your presentation, sir, warning the group of possibly nutritional risks in following the diet? This is not in a selected, highly motivated, carefully monitored group, but the general public, either in somebody's experiments or as a result of it. Dr. Feingold says it is not a risk. Where does the truth lie? What is your present view on this?

Dr. Kerr. I have no experience working with these children, but I think as a rule for society, any time someone changes their pattern of eating, and particularly if they restrict the number of foods that have been previously eaten, there are risks unless somebody can assure that the nutrients that are no longer provided in those foods are still present in the food now eaten.

That takes supervision, and it takes a great deal of knowledge about intake of foods. So I would say, a priori, any time diets of families are changed, unless the changes are supervised, there is a risk involved.

Dr. Kolbye. Dr. Feingold?

Dr. Feingold. I know that criticism may hold—that is why I take the position that I indicated. You will find that some children require the first part of the diet in order to get response. But the percentage is smaller. So there is no risk at all, I say, because there is not a single food you can name that the children are not permitted to have; it is just that they have no color and flavor.

They can have cake; they can have ice cream; they can have candy—anything. There is nothing they are deprived of. Why make a mountain out of a molehill?

Dr. KERR. Well, I make a small mountain, because I had recent contact with a child that a physician put on a restricted diet with the very best intentions. It was an unwise diet, and was monitored very poorly. Without his supervision, I think, many families might do worse.

Dr. KOLBYE. I think I was down to going twice, so I will start the cycle over again, because I do not wish to turn anybody off if they have any additional comments. So I will repeat the bidding. Going once, going twice, going thrice. I would like to thank our guests and visitors very, very much.

I would like to ask the members of the interagency panel to remain in the room.

I promise that I will let you go in about 20 mintues.

[Thereupon, at 3:55 p.m., the open session of the meeting was adjourned.]

FIRST REPORT OF THE
PRELIMINARY FINDINGS AND RECOMMENDATIONS
OF
The Interagency Collaborative Group on Hyperkinesis

Submitted to
The Assistant Secretary for Health
U.S. Department of Health, Education and Welfare

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INTRODUCTION

The Interagency Collaborative Group on Hyperkinesis (ICGH) held its first organizational meeting on July 31, 1975 at the Parklawn Building. In attendance at the meeting were representatives from the Bureaus of Food and Drugs, Food and Drug Administration, National Institute of Education, National Institute of Mental Health, National Institute for Child Health and Human Development, National Institute of Neurological, Communicative Disorders and Stroke, and the Bureau of Community Health Services.

As a result of the exchange of information between the scientists on the Interagency Group, the Assistant Secretary for Health set forth the functions which the ICGH should perform. These are:

a. Exchange information, coordinate expertise, evaluate existing data from ongoing research and review proposed research for the purpose of making findings and recommendations to the Assistant Secretary for Health concerning hyperkinesis and dietary factors.

    1. The findings shall speak to the significance of available data, the relevant issues, parameters studied and criteria employed, in order to resolve whether or not dietary modifications contribute significantly to a reduction of symptoms in hyperkinetic children.

2. Recommendations shall include the description of needed research, the parameters to be studied, the recommended experimental design, the suggested priority of effort, and funding mechanism to be employed.

b. The ICGH shall, from time to time, seek the advice and guidance of recognized investigators in the area of hyperkinesis.

c. The ICGH shall report its preliminary findings and recommendations to the Assistant Secretary for Health by October 31, and shall meet, when deemed appropriate by its chairman, to fulfill its mission of expediting the resolution of the relevant issues.

d. The ICGH should consider the means by which suitable research proposals should be solicited and funded. The group should function to expedite, but not circumvent, existing review and funding mechanism.

At subsequent meetings, subcommittees were organized to research and discuss these various functions.

On September 30, 1975, a conference was held to discuss research in hyperkinesis (see Appendix for Report) with invited speakers from several universities. These speakers included:

Keith Conners, Ph.D.
Department of Psychiatry, School of Medicine
University of Pittsburgh

Esther Wender, M.D.
Department of Pediatrics, College of Medicine
University of Utah

George Kerr, M.D.
Department of Nutrition, School of Public Health
Harvard University

J. P. Harley, Ph.D.
Department of Neurology
University of Wisconsin

Richard J. Schain, M.D.
Division of Pediatric Neurology
University of California - Los Angeles

Ben Feingold, M.D.
Department of Allergy
Kaiser Permanente Medical Center

Sheldon Margan, M.D.
Department of Nutritional Sciences
University of California - Berkeley

Bernard Weiss, Ph.D.
Department of Radiation Biology and Physics
University of Rochester

Morris Lipton, M.D.
Department of Psychiatry, School of Medicine
University of North Carolina

Additional meetings of the ICGH on October 15, 22 and 31 were concerned with the preparation of the preliminary findings and recommendations to be presented to the Assistant Secretary for Health. It is anticipated that the ICGH shall continue to meet in order to complete the preparation of detailed protocols for carrying out the research studies which are recommended in this preliminary report.

DEFINITIONS

The "hyperkinetic behavior syndrome" refers to a complex group of problems, occurring primarily in children, which are manifested in a manner extremely distressing to families and teachers, and to children themselves. This type of disturbance, which is also called "minimal brain dysfunction" (MBD), hyperkinetic syndrome, or hyperkinesis has no known single cause or simple answer for such problems. The major symptoms are an increase of purposeless physical activity and a significantly impaired span of focused attention. The inability to control physical motion and attention may generate other consequences, such as disturbed mood and behavior within the home, at play with peers, and in the schoolroom.

In its clear-cut form, the overt hyperactivity is not simply a matter of degree of activity but of quality or type of physical motion. The physical activity appears driven, so that the activity is beyond the child's control, as compared to other children. The child is readily distracted, racing from one idea and interest to another, but unable to focus attention. The Diagnostic and Statistical Manual of the American Psychiatric Association classified these disorders as:

IX. BEHAVIOR DISORDERS OF CHILDHOOD AND ADOLESCENCE (308)

308* Behavior disorders of childhood and adolescence
(Behavior disorders of childhood)

> *This major category is reserved for disorders occurring in childhood and adolescence that are more stable, internalized, and resistant to treatment than transient situational disturbances (q.v.) but less so than Psychoses, Neuroses, and Personality disorders (q.v.). This intermediate stability is attributed to the greater fluidity of all behavior at this age. Characteristic manifestations include such symptoms as overactivity, inattentiveness, shyness, feeling of rejection, overaggressiveness, timidity, and delinquency.
>
> 308.0* Hyperkinetic reaction of childhood (or adolescence)
>
> *This disorder is characterized by overactivity, restlessness, distractibility, and short attention span, especially in young children; the behavior is caused by organic brain damage, it should be diagnosed under the appropriate non-psychotic organic brain syndrome (q.v.).

The working revision of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-III) has changed the emphasis from hyperactivity _per se_, as the core symptom of the hyperactive reaction of childhood (308.0), to attentional deficits as the central component of this disorder; e.g. attention deficit disorder (314.00) with or without hyperactivity.

DIAGNOSIS OF HYPERKINETIC DISORDERS

In the diagnosis of hyperkinetic behavioral disturbances, it is important to note that similar behavioral symptoms may be due to other illnesses or to relatively simple causes. Essentially healthy children may have difficulty maintaining attention and motor control because of a period of stress in school or at home. It is important to differentiate the hyperkinetic child from the child whose inattention and restlessness may be caused by hunger, poor teaching, overcrowded classrooms, or lack of understanding by teachers or parents. Frustrated adults reacting to a child who does not meet their standards can exaggerate the significance of occasional inattention or restlesness. Above all, the normal ebulience of childhood should not be confused with the very special problems of the child with hyperkinetic behavioral disorders.

The diagnosis of hyperkinesis is clearly best made by a skilled observer. Unfortunately, there is no single diagnostic test. Accordingly, the specialist must comprehensively evaluate the child and assess the significance of a variety of symptoms. Casual and contributory factors, both permanent and temporary, such as environmental stress, must be considered. Special dysfunctions such as certain epilepsies, schizophrenia, depression or anxiety, mental retardation or perceptual deficiencies must be distinguished. The less severe and dramatic forms of hyperkinetic disorders also require careful evaluation. Adequate diagnosis may require the use not only of medical, but os special psychological, educational and social resources.

PREVALENCE

Estimates of the prevalence of the hyperkinetic syndrome have ranged from a conservative estimate of 3% to a high estimate lf 15% (Schrag, P. and Divoky, D. The Myth of Hyperactive Child, Pantheon Book, 1975, p. 35).

The most frequently cited prevalence estimates are given as ranging between 5-10% (Wender, P. Minimal Brain Dysfunction in Children, Willy & Sons, 1971, p. 62). In reviewing studies related to the 5-10% prevalence estimate, Wender has drawn from data obtained by Hussy, Prechtl and Stemmer, Stewart, et al, and from a survey done in Montgomery County, Maryland.

A conservative estimate would be that moderate and severe hyperkinetic behavioral disorders are found in about 3 out of 100 elementary school children--an estimate that would vary somewhat in different communities. (Report of the Conference on Use of Stimulant Drugs in Treatment of Behaviorally Disturbed Young School Children.) More males than females are affected, as is true in a number of childhood ailments.

Children with the hyperkinetic syndrome are clinically defined as limited to those of at least low normal or high intelligence. A near majority are reported to have had behavorial problems since infancy. There is a smaller group of more severely afflicted children upon whom most studies have focused. they may show hyperactivity and reduced attention which ranges in degree from mild to severe, with or without associated physical signs or special learning impairments; some have complex behavioral and personality problems. A significant number of hyperkinetic children have special learning and reading difficulties, along with the major hyperkinetic symptoms.

The range in prevalence figures reported could reflect actual differences in the populations studied or a number of other factors, including difference in socioeconomic status, geography, definitions and terminology from study to study, and any bias or selection by the investigator collecting the data. Details concerning these factors and their effect of estimates of prevalence have been provided by Minskoff, J. G., in Differential Approaches to Prevalence Estimates of Learning Disability. *Annals. of the New York Acad. Sciences* 205: 139-145, 1973.

Just as the estimates for the prevalence of the hyperkinetic syndrome have varied, so too have the estimates of the prevalence of the use of medication for the treatment of this disorder. In this regard, estimates of the prevalence of medication have ranged from 2% (Krager, J. M. and Safer, D. J., Type and Prevalence of Medication Used in Treatment of Hyperactive Children, *New Eng. Jour. Med.* 291:118-1120) to 2-4% (Sprague and Sleator, *Pediatr. Clinics of North America*, .973) to a high of from 10-15% (in some school districts) as cited by Walker (Walker, S., Drugging the American Child; We're too Cavalier about Hyperactivity. *Psycol. Today*, Dec. 1974). It seems clear that the more conservative prevalence estimate of 2-4% of school age children as receiving medication for the treatment of the hyperkinetic syndrome represents the more valid national estimate.

FACTORS RELATED TO HYPERKINETIC DISORDERS

The present state of scientific literature indicates the perplexing problem of identifying definitive causes. The disorder has been ascribed to biological, psychological, social or environmental factors, or a combination of these. There is speculation that the core set of symptoms, i.e., those affecting control of attention and motor activity, may have their origin in events taking place before the child is born, during the birth process, or they may be related to some infection or injury in early life.

The hyperkinetic syndrome was originally described in children who had suffered known injury to the brain (Strauss and Lehtinen). Previously normal children who experienced severe physical trauma, or encephalopathy due to measles or influenza, for instance, sometimes afterward displayed disinhibited overactive behavior, stimulus-binding, and attentional defects.

That the converse is necessarily true, that all children who show any or all such symptoms must have experienced damage to their brains, is clearly contrary to logic. In fact, there is almost no information available on this possible relationship between neuropathologic changes of the sort identifiable by current techniques, and hyperkinetic behavior disorders except in rare and specific situations. The neuropathologic basis of the hyperactivity syndrome is simply unknown.

However, a discussion of some of the observed relationships between the occurrence of hyperactivity in children and social, environmental and biochemical factors, nutritional status, allergy or intolerance to substances, and exposure to toxic substances may contribute to our understanding of various components of the hyperactive child syndrome.

A. Social Factors: Almost all those who have discussed the etiology of deviant behavior syndromes assign importance to social aspects of the child's environment. The child's relationship with parents, teachers, siblings, peers and the culture at large are unquestionably significant contributors to his or her behavior, whether it be viewed as within or outside normal limits. Tensions arising from poor social relationships can trigger hyperactive behavior which in extreme form can contribute to further deterioration of the social input in a depressing downward spiral familiar to many teachers and parents. As mentioned earlier in this report, however, caution must be exercised in employing simple unimodal explanations of the effects of increased activity on socialization. Patterson, G. R., Jones, R., Whittier, J. and Wright, M. A. A behavior modification technique for the hyperactive child (Behav. Res. Ther., 1965, 2: 217-226) have proposed that a curvilinear relationship exists between activity levels and acquisition of socially acceptable behaviors, with moderate to high levels of activity correlating with social success.

Many workers have described significant success with social-behavioral approaches to treatment, and some insist that behavioral intervention is either universally effective or at least the most successful approach (Gelfand, D. M. and Hartmen, D. P. Behav. Therapy with Children, A review and evaluation of research methodology, In Craziano, A. M. (Ed) Behavior Therapy with Children, 1971, Chicago, Ill., Aldine Pub. Co.). Better results may be obtained when the entire family, teachers and peers are included in such interventions, again emphasizing that the social context in which the hyperkinetic child lives and grows is crucial. Even though an exclusively social-behavioral view of hyperkinetic behavior is undoubtedly incomplete (and at variance with data considered in other sections of this report) an awareness of this fundamental truth must permeate all discussions of causes, model mechanisms, and treatment interventions in relation to hyperkinetic behavior.

Food, nutritional status, and dietary intervention have significant familial and social components (Kallen, S. J. ed. Nutrition, Development and Social Behavior - USDHEW, PHS, DHEW Publication No. (NIH) 73-242). Introduction of special diets for a member of the family creates changes in the social interactions of members of the family. With regard to hyperkinetic children, it has been repeatedly pointed out that the child welcomes diet intervention and reminds other family members of the importance of food restrictions to his behavior. (Stroufe and Stewart, L. A. Stroufe and M. A. Stewart, Treating Problem-Children with Stimulant Drugs, New Engl. J. Med. 289: 407-413, 1973), have described some of the changes in family structure that may occur during drug therapy for hyperkinesis: the child is less responsible for his own behavior and the parent avoids a degree of child-rearing responsibility.

B. Biochemical Factors: Hyperkinetic behavior is described as an aspect of many neuropsychological disorders. It is important to distinguish hyperkinesis from other aspects of these disorders, because they may involve separable biochemical dysfunctions and may respond to different pharmacological management. Hyperkinetic behavior may be associated with actual brain damage, as in perinatal anoxia and in the disorders described consequent to the 1917-1918 epidemic of encephalitis. In experimental animals, increases in spontaneous motor activity result from selective electrolytic and chemical lesioning, prenatal x-rays, and neonatal carbon monoxide exposure. The diversity of experimental treatments which produce hyperactive animals has complicated biochemical interpretations.

Briefly, two biochemical hypothesis for hyperkinesis have been proposed: (1) biochemical pathways of arousal are not functioning normally and hyperkinetic children are actually underaroused or (2) biochemical pathways of behavioral inhibition are not functioning fully.

The first hypothesis is supported by the expected action of the amphetamines and methylphenidate to increase behavioral arousal. If it is correct then hyperkinetic children would be predicted to demonstrate underarousal biochemically and physiologically. There are reports of indicators of underarousal in such children -- such as galvanic skin response, auditory evoked response, and sleep EEG. So far, however, no differences have been found between hyperkinetic and normal children in levels of some urinary catecholamine metabolites or serotonin function in platelets or in rate of metabolism of the amphetamines.

A problem with this hypothesis has been that experimentally increased motor activity is associated with increased neurochemical function of catecholamine pathways linked to behavorial arousal and those pathways are also stimulated by amphetamine and methylphenidate.

The second hypothesis of decreased function of pathways linked to behavioral inhibition has not been extensively investigated.

C. Nutritional Factors: One facet of biochemically induced hyperactivity is probably associated with many diverse influences related to nutritional factors. Such an influence can, in some instances, be related directly to the quality and/or the quantity of bioavailable nutrients in the diet, or to the time relationships of the available supply of specific nutrients in response to the body's demand for nutrients and energy under the various circumstances of daily activity. In some instances, metabolic patterns differ substantially from individual to individual and as such, may increase the susceptibility of a particular individual to an excess of one factor or a deficiency of another.

The subsequent discussion on the possible role of food components in modification of neurological or behavioral changes should be prefaced by several considerations. A portion of the behavioral aberration in hyperkinesis may be dependent on psychological rather than metabolic or biochemical factors; however, given the primitive state of knowledge about this condition, metabolic abnormalities as causative factors in hyperkinesis remain distinct possibilities. Metabolic abnormalities may be of either a quantitative or qualitative nature. The pathways of metabolizing certain compounds may be essentially normal in the hyperkinetic child, but the quantities of compounds needed to produce a specific effect may be substantially higher or lower than those needed by the vast majority of the population.

Thus changes in levels of a stimulant such as caffeine might have little effect on normal people but could produce pronounced behavioral changes in hyperkinetic subjects. Qualitatively, there may simply be alternate metabolic pathways present in the hyperkinetic child that result in formation of abnormal products from precursors that are in no way harmful to the normal population.

Alterations in food intake can involve changes in the level of ingestion of a number of food constituents that have potential effects on neurological function, or on behavior. Food constituents may show these influences through deficiencies of nutritionally required constituents or through excesses of these or other components.

It has been hypothesized that diet can affect brain neurotransmission by altering the availability of precursors. These precursors, the amino acids tryptophan (precursor for 5-hydroxytryptamine) and tyrosine (precursor for norepinephrine and dopamine) and choline (precursor for acetylcholine) are normal constituents of dietary protein.

The evidence for dietary control of the rate of synthesis of the monoamines and acetylcholine to which they are converted comes from the work of Wurtman, et al., (Wurtman, R. J., and Fernstrom, J. D., Nutrition and the Brain in the Neurosciences 3rd Study Program, ed. by Schmitt, F. O., and Worden, F. G. pp. 685-693, MIT Press, Cambridge, 1974): (Wurtman, R. J., Catechol Synthesis: Control by Brain Tyrosine Concentration, Science 185: 183-184, 1974); (Wurtman, R., Abst. 5th Annual Mtg. Soc. Neuroscience, 1975).

For example, peripheral administration of tryptophan or tyrosine to rats increases the amount of these substances in the brain, and results in a significant increase in the rate of synthesis of brain 5-hydroxytryptamine and catecholamine (norepinepherine and dopamine), respectively. It has also been shown that it is not only the absolute amount, but also the relative proportion of these amino acids in the diet which determine their effect on monoamine synthesis. More especially, amino acids which compete with tryptophan and tyrosine for uptake into the brain can lower their entry into the brain and thus decrease 5-hydroxytryptamine and catecholamine synthesis, respectively. (The amino acids, i.e. tryptophan, tyrosine, phenylalanine, leucine, isoleucine, and valine, share a common uptake system and thus compete with each other for entry into the brain.) Thus, the amounts of any of these amino acids in the diet (and also any other dietary factors which can alter endogenous amino acid levels) can influence brain monoamine synthesis.

Other agents, such as administration of insulin (2 units/kg) or consumption of a carbohydrate meal by rats, which has been found to cause an increase in plasma tryptophan, and a decrease in levels of other amino acids, results in an increased level of brain tryptophan and 5-hydroxytryptamine. (Wurtman, R. J. and Fernstrom, J. D. Nutrition and the Brain in the Neuroscoeiences 3rd Study Program, ed. by Schmitt, F. O. and Worden, F. G., pgs. 685-693. MIT Press, Cambridge, 1974).

Other dietary factors can indirectly influence the availability of precursor amino acids for brain monoamine synthesis. This is especially true for free tryptophan, which is transported in the blood loosely bound to plasma albumin. (Paoletti, R., Sirtori, C., Jr., and Spano, P. F. Clinical Relevance of Drugs Affecting Tryptophan Transport, Ann. Rev. Pharmacol. 15: 73-81, 1975).

Since free fatty acids (FFA) are also bound to plasma albumin, they can displace the free tryptophan that is not chemically bound, from the plasma albumin, and any dietary factor leading to altered FFA levels can potentially alter the amount of tryptophan available for entry into the brain and conversion of 5-hydroxytryptamine. For example, the decreased FFA levels induced by glucose ingestion in humans decreased the percentage of free tryptophan by about 35%. Interestingly, all stimulant drugs used in the treatment of the hyperkinetic syndrome, including caffeine, has been shown to increase serum or plasma FFA in animals and/or man, and the administration of amphetamine to animals has been shown to produce up to a 3-fold increase in brain tryptophan levels. Parenthetically, it may be mentioned that salicylates are also capable of displacing tryptophan from albumin. (Paoletti, R., Sirtori, C., Jr., and Spani, P. F., Clinical relevance of Drugs Affecting Tryptophan Transport. *Ann. Rev. Pharmacol. 15*: 73-81, 1975).

The practical effect on human behavior of altered brain monoamine synthesis due to dietary factors which alter the availability of precursors for monoamine synthesis is difficult to assess. Relatively large doses of monoamine precursors have been used with variable success in treating depression, (Carroll, B. J., Monoamine Precursors in the Treatment of Depression. *Clin Pharm. Ther*. 12: 743-761, 1973), although relatively large doses were used. The administration of large doses of tryptophan is being investigated for use as a soporific, and for treatment of MBD.

In addition to direct effects on neurotransmitter levels, the presence or absence of food components may produce a number of neurological or behavioral effects. The mechanism of these is relatively less clearly understood. For example, deficiencies of many of the B-complex vitamins produce effects on the central nervous system and on behavior, possibly through their role as coenzymes. Also not clearly understood are the role of trace minerals such as manganese, copper, zinc, or iron in altering behavior. However, it is known that behavioral changes develop with iron deficiency anemia that are readily reversed on treatment with iron. (Read, S. M., Anemia and Behavior, Mod Prob. Pediat. 14:89-202, 1975). Manganese deficiencies in animals is associated with control of motor activity. (Hurley, L. S. and G. J. Everson, Proc. Soc. Exp. Biol. Med., 102:360, 1959).

The influence of these dietary factors may occur in several ways:

1. Direct dietary deficiency as in iron, manganese, copper or zinc. It is known that the diet in the U. S. can easily be deficient in zinc and iron unless foods are selected with substantial care.
2. An abnormally high requirement of some children for certain vitamins such as niacin, folic acid or pyridoxine. Niacin and pyridoxine are normally present in the diet in quantities adequate for most of the population. The adequacy of folic acid in the diet of some of the population is open to question.

3. Abnormal metabolism of any of these vitamins or minerals in a manner that effects chemicals which regulate behavior.

Metabolically induced hyperactivity has also been linked to the occurrence of hypoglycemia. In those individuals who are susceptible to reactive (post absorptive) hypoglycemia, the relative proportions of energy yielding nutrients can affect the occurrence of symptoms. In these individuals diets high in carbohydrates, especially for breakfast meals, promote hypoglycemic symptoms which include hyperactivity, irrationsl behavior, and inability to concentrate, (William, R. H. Textbook of Endocrinology, W. B. Sanders Co., Phila. Pa. p. 640, 1974).

The occurrence of such symptoms can be avoided by the consumption of diets high in protein and fat relative to carbohydrates. That the condition is influenced by the consumption of high levels of carbohydrates is shown by the fact that the symptoms are frequently avoidable during fasting. The assumption is that the absorption of carbohydrates stimulate the secretion of insulin in either excessive amounts or that such insulin is not subjected to normal metabolism. In either case, the levels of insulin remain high after blood glucose levels have returned to a normal range. Subsequent reduction of blood glucose results in the occurrence of hypoglycemia symptoms. Stimulation of catecholamine secretion is beneficial to such individuals in that insulin levels are lowered and the utilization of glucose by the muscles is reduced.

D. Allergy or Intolerance to Substances: Unusual reactions to many substances may induce hypersensitivity or an intolerance phenomena. These inducing factors may include biochemical entities which are ingredients present in the foods themselves, or natural or artificial ingredients which are added to other foods as agents to aid in the processing, flavoring, coloring or preservation of foods. Such natural or artificial ingredients are generically referred to as food additives. The phenomena induced may range from demonstrable antibody-mediated allergic reactions to the less well understood intolerance phenomena which reflect non-antibody-mediated manifestations more properly characterized as toxicity reactions. Physical manifestations of such phenomena may include obvious signs of eczema, urticaria, asthma, etc., to less obvious manifestations which can include malaise, fever, and neurobehavioral changes.

A relationship between an allergic or hypersensitive reaction to artificial food additives and hyperkinesis has been postulated by Feingold. However, while a variety of allergic or sensitizing reactions ranging from urticaria (hives) to severe asthma have been reported to occur in susceptible people following ingestion of certain synthetic colors that are used in foods and drugs (Chafee, F. H. and Settipane, G. S., 1967, *J. Allergy* 40:65; Feingold, B. F., 1968, *Ann. Allergy* 26:301; Lockey, S. D., 1959, *Ann. Allergy* 17:719; Samter, M. and Beers, R. F., 1967, *J. Allergy* 40:281), there is presently no evidence to indicate an association between an allergic or hypersensitive response to these agents and hyperkinesis. The mechanism of hypersenitivity to aspirin is not well understood. Because aspirin is a low molecular weight compound, its sensitization effect has been postulated to be that of an incomplete antigen or hapten. The hapten is a chemically active substance of low molecular weight that does not induce an immune response by itself but by combining with larger molecules called "carriers" becomes immunogenic (Sell, S. - *Immunology, Immunopathology, and Immunity* - Harper and Row, New York, 1972). Most of the patients studied were persons showing allergic or sensitivity reactions to acetyl salicylate. Aspirin intolerance has not been found consistently to be generalized to salicylate intolerance since many aspirin intolerant patients do not react to sodium salicylate, salicylic acid esters, choline salicylate, or thioaspirin (M. Samter, Hosp. *Prac*. 85-90, 1973). Of Samter and Beers' 182 aspirin sensitive patients with asthma and sometimes urticaria, approximately 23% had sensitivities to foods and drugs. Fourteen patients were found to be sensitive to the dye tartrazine. Similar findings of tartrazine have been reported by other investigators although the percent of aspirin sensitive persons who are sensitive to tartrazine has been reported as greater than that seen in the initial series (Juhlin, M., Michaelsson, G., and Zetterstrom, O.-Urticaria and Asthma Induced by Food-and-Drug Additives in Patients with Aspirin Hypersensitivity, J. Allergy and Clin. Immunol. 50:92-98, 1972). Cross reactivity of aspirin sensitivity persons has been reported with benzoates (Chaffe, E. H. and Settipane, G. S.: Asthma Caused by FD&C Approved Dyes, J. Allergy 40:65, 1967), although this is much less frequent than cross-reactivity to tartrazine (Anonymous Aspirin Intolerance - Lancet, Annotations, Sept. 14, page 618, 1968).

Cross reactions have been reported for other azo dyes and benzoates (G. Michaelsson and L. Juhlin, Urticaria Induced by Preservatives and Dye Additives in Foods, Br. J Dermatology 88: 525-532, 1973). The mechanism responsible for the cross-reactivity of aspirin, tartrazine and other azo dye sensitivity or intolerance is not established.

Tartrazine, if taken orally, undergoes azo-reductive cleavage in the gastrointestinal tract and in humans results in the excretion in 48 hours of sulfanilic acid equivalent to the total amount of tartrazine ingested. (Jones, R., Ryan, A. J., and Wright, S. E.: The Metabolism and Excretion of Tartrazine in Rat, Rabbit, and Man) Food Cosmet. Toxicol. 2:447, 1964).

Samter and Beers have suggested that tartrazine undergoes biotransformation in a limited number of persons which may account for sensitivity reactions in a small number of persons (Samter, M. and Beers, R. E.: Concerning the Nature of Intolerance for Aspirin - J. Allergy 40:281-293, 1967).

Because of the possibility that an in vivo formed metabolite of the food additive is responsible for the hypersensitivity response sublingual or cutaneous testing with the compound may yield false-negative results. It is also possible that physical alterations of foods during processing or cooking may produce a change in the structure of the additive and be responsible for false-negative results on testing of the unchanged additive.

Because of the difficulties of determining food allergies with subcutaneous and sublingual testing, elimination diets and challenges with the food or food component in question are tried by clinicians. These trials are basically very similar to many of the studies proposed to evaluate the effects of food colors and flavors on hyperkinesis.

TOXIC REACTIONS

The influence of food on neurological functions or behavior can occur through chemical constituents present in food other than those nutritionally required. There are a number of psychoactive components in foods such as nutmeg, or ergot, which may be consumed by eating food contaminated with a fungus. In susceptible individuals substantially smaller quantities of these compounds than are usually required may produce central nervous system effects.

Lead Toxicity: Research on lead toxicity in children has demonstrated involvement with both the peripheral and central nervous system. Through the years, this area of research has been intensely investigated and the literature has been the subject of two recent reviews (Wiener G. Varying Psychological Sequelae of Lead Ingestion in Children, Public Health Rep., 85: 19, 1970, and Waldron, H. A. and D. Stofen, Subclinical Lead Poisoning, New York Acad. Press, 1974). Among the symptoms observed in individuals who contracted lead toxicity during childhood are hyperactivity, impaired learning, heightened aggressiveness, emotional instability and deficiencies in motor coordination. These changes in central nervous system function appear to be permanent. However, some have responded to drug therapy and there is some evidence that treatment with chelating compounds was useful. The impact of subclinical lead toxicity on learning and behavioral disorders has been studied. (Moncrieff, A. A., et al., Lead Poisoning in Children, Arch. Dis. Child, 39:1, 1964 and Millar, J. A., et al., Lead and α-Amino-levulinic Acid Dehydratase Levels in Mentally Retarded Children and in Lead-Poisoned Suckling rats. Lancet II: 695, 1970).

The results of these studies are not conclusive and comparisons are difficult due to methodology differences. Epidemiological data on the other hand have shown correlations between lead poisoning and hyperactivity, deficits in motor coordination and learning. (De La Burdee, B., Does Asymptomatic Lead Exposure in Children have Latent Sequelae? J. Pediat. 81: 1088, 1973 and David, O., Lead and Hyperactivity, Lancet I:900, 1972.)

A review of data published in the literature shows that lead toxicity has a significantly greater impact on the very young (less than six months of age) compared to older children. (Belmont, L. and H. C. Birch. The relationship of time life to behavior consequence in brain damage: The organizational of factual form experience in brain injured adults, J. Nerv. & Men. Diseases, 137: 489, 1960; Airborne lead in perspective, Washington, D. C., National Academy of Sciences, 1972 and Greensbaum, J. V. and L. A. Laurie, Encephalitis as a Causative factor in behavior of disorders of children, JAMA 136:923, 1948).

SAFETY TESTING OF FOOD ADDITIVES

Throughout history humans have ingested a variety of dietary substances either for their intrinsic nutritional value or for the purposes of enhancing appearance, flavor, preparation or preservation of foods. These included condiments, spices, pepper and salt.

Natural coloring and flavoring agents were used in food products until such time as their supply became limited in relation to demand. Chemists, then asked to provide cheaper substitutes, analyzed the complex chemistry of flavors to determine characteristic moieties which could be isolated or synthesized and combined to reproduce the flavor desired. Natural substances were first used as coloring agents and included calcium carbonate, charcoal and vegetable extracts. When organic dyes were found which would mimic reds, blues, yellows and greens, they gradually came into use.

In the United States prior to 1958, pre-clearance for food and color additives was not mandated. While the Food, Drug and Cosmetic Act of 1938 prohibited the addition of poisonous or deleterious substances to food, the lack of pre-clearance requirement imposed upon the Food and Drug Administration the responsibility to determine whether a food additive was harmful. This was done only when there was an indication that the additive might be harmful. In the case of the synthetic organic colors (so-called coal tar colors) the law mandated that FDA test these colors for their ability to cause harm and that FDA establish certification procedures for these colors on a batch basis. A number of such colors were removed from use. In essence then, prior to 1958, the FDA was required to establish that compounds were harmful on the basis of legally satisfactory evidence before they could be removed from use.

The food and color additive amendments of 1958 and 1960, respectively, changed the legal philosophy. Pre-clearance was required. This shifted responsibility to the user for the prior establishment of safety. These amendments also set forth the principle of "safe conditions of use". This, in essence, was recognition of the generality that any chemical (even those which are essential to life and not considered to pose any hazard) may be unsafe, unless used under conditions which are proper for its safety. The food additive amendment contained a "grandfather" clause which in effect, without the need for pre-clearance, permitted those food additives that were in actual use prior to January 2, 1958, and which were Generally Recognized as Safe [GRAS] or were considered safe on the basis of scientific procedures or long experience of use to continue in use. The 1960 color additive amendments, while requiring safety testing for all colors, recognized the need and provided for an interim listing of colors commercially established at the time of enactment of the law, with the proviso that this would not apply to those colors subject to certification for which no batch had ever been certified and further, that for any color listed on an interim basis safety studies were to be initiated promptly, evidence to this effect being required within two and one-half years.

During the period of time (1958-1960) and subsequently until 1970, FDA was confronted with a series of pragmatic problems involving priorities for resolving problems on a "worst first" basis, in view of limited resources. It was recognized that there were countless hundreds of "additives" and food ingredients that had enjoyed a long history of apparent safe use.

The GRAS list, created after review by toxicologists nation wide, established those additives which were considered as being safe without further safety testing for their intended use. This permitted FDA to concentrate on potential problem substances, not considered GRAS, many of which become classified as food additives, for which additional safety evidence was demanded and received before FDA could grant approval for use.

For the past few years, FDA has funded a major safety review of substances on the GRAS list by a select committee of the Federation of American Societies for Experimental Biology, to determine if additional safety evidence is needed or if restrictions on currently permitted uses are indicated. Currently underway is a similar review for flavors.

In general, safety testing depends upon the fact that as the exposure dose is decreased, toxicity effects also decrease and a dose is finally established at which "no effects" are produced. Usage levels which are permitted in food are then set based on the "no-effect" level into which has been incorporated an additional safety factor.

To some extent the kinds of safety data required by a preclearance review to establish the safety of a proposed food or color additive are also directly related to the anticipated degree of human exposure likely to result if such use is permitted. For significant direct additives, i.e., those which are intentionally added to food, complete toxicological workup is required. For indirect additives, i.e., those which have some potential for transfer into foods by virtue of their use in the manufacture or maintenance of food packaging materials and processing equipment, toxicity testing requirements may be reduced. In particular, only short-term animal testing might be required to determine if a substance was highly toxic where essentially no residues from migration or extraction is expected to occur in food.

At present, a complete toxicological workup includes a variety of chemical tests to determine the composition and purity of the substance in question and then a variety of feeding experiments in test animals to determine the quantitative strength of all qualitative toxic effects that the substance can be demonstrated to cause in animals receiving large doses daily over extended periods of time. For example, lifetime feeding studies are required in two different rodent species - usually the mouse and the rat. These tests are designed to establish an "effect" level, if possible. FDA looks for a variety of effects such as poor growth and development, visible signs of neurological abnormalities, including those likely to be associated with chemically-induced lesions on the motor and sensory centers and pathways of the nervous system. Animals are observed for abnormalities of gait, righting reflexes, ingesting reflexes, and tremors. They are also observed for any other visible palpable signs of disease such as skin, ear and eye abnormalities, gastrointestinal disturbances, and tumors. After death, the animals are subjected to a complete autopsy and extensive histopathological examination to determine cause of death, compound related diseases, and any incidence of tumors including malignant neoplasms (cancer). The data are then analyzed statistically when differences between test and control animals are seen, to determine the statistical significance of those observed differences. One rodent lifetime study, the rat study, is designed so that the animals used have been exposed to the test material over their lifetimes beginning with exposure in utero. This insures that they have been exposed to any substance likely to cross the placenta. In multi-generation studies, parents of successive generations are observed for reproductive performance, fertility and viability and growth of offspring. Successive mating serves to determine whether offspring who were exposed in utero are capable of reproducing their own normal offspring. These multi-generation reproduction studies (usually on the rat) usually involve two litters per generation over three generations.

Other specific tests, such as teratology studies, are performed to see if a substance can be demonstrated to be capable of inducing birth defects. Reproductive testing, in general, will detect decreased fertility, increased fetal death, birth defects, decreased survival and well-being of offspring at birth after being exposed in utero; and abnormal growth and development during the lactation stage with the maternal animals still exposed to the test substance. These required reproduction protocols will obviously measure effects of the substance tested on the entire spectrum of physiological functions involved with the maternal animals still exposed to the test substance, and on the entire spectrum of physiological functions involved with reproduction. The physiology of reproduction involves the integration of complicated metabolic, hormonal, neurological and behavioral processes and thus serves also to detect more subtle disturbances of higher centers.

TREATMENT PROGRAMS

Although the symptoms of hyperkinesis in children may range from mild to severe and have poorly understood causes and outcomes, the need for treatment or special interventions remains.

Several approaches to treatment now appear to be helpful. Special classes and teachers can be directed to specific learning disabilities and thus restore the confidence of the child who experiences chronic failure. Modification of behavior by systematic rewarding of desired actions has been reported to be useful in some children. Elimination of disturbing influences in the family or classroom through counseling may often tip the balance, and a happier child may show improved control and function.

Drugs: There will be children for whom efforts such as those described above are not sufficient. Their histories and their examinations reveal symptoms of such a driven nature that skilled clinicians undertake a trial of medical treatment. Drugs do not "cure" the condition, but the child may become more accessible to educational and counseling efforts. Over the short term and at a critical age, medication can provide the help needed for the child's development.

Stimulant medications are beneficial in only about one-half to two-thirds of the cases in which trials of the drugs are warranted. The stimulant drugs are considered to be the first and least complicated of any drugs to be tried. Other drugs, such as the so-called tranquilizers and anti-depressants, are generally reserved for a smaller group of patients. Without such specialized medical therapy, the developmental and educational consequences for these children are clearly severe. In such cases the aim is not to "solve problems with drugs," but to put the severely handicapped child in a position to interact with his environment to the extent that his condition permits.

Response to stimulant medication cannot be predicted in advance. Fortunately, the issue can be resolved quickly. When stimulants are given in adequate doses, a favorable response occurs fairly rapidly, and is unmistakeably the consequence of the drug. Thus, if an adequate test of pharmacotherapy (a few days or weeks) produces only doubtful benefits or none at all, treatment can be promptly terminated. The physician will, of course, adjust dosage carefully to assure an adequate therapeutic trial. It should be pointed out, however, that not all affected children require medication and that of those who do, not all respond.

When the medication is effective, the child can usually modulate and organize his activities more in the direction he wishes than previously. The stimulant does not slow down or suppress the hyperkinetic child in the exercise of his initiative, nor does it make him feel overstimulated, or out of touch with his environment. Although their exact mechanism of action is not known, stimulants do not provide a chemical strait-jacket. They do not act as a sedative. Rather, they appear to mobilize and to increase the child's abilities to focus on meaningful stimuli and to organize his bodily movements more purposefully.

The most typical side-effects of the stimulant medications, loss of appetite and sleep difficulty. diminish over time and can be adequately controlled by adjusting the prescribed dosage and/or the time during the day when the drugs are given. No medication should be given for a longer period of time than may be required and it is good clinical practice, therefore, to discontinue medication for a few weeks once or twice a year to determine whether or not the child still requires medication. If there is no recurrence of the symptoms of the hyperkinetic syndrome, medication should be discontinued.

In a recent long-term study of methylphenidate, it was reported that 26% of 60 MBD children no longer required medication after two years of treatment. (Sleator, K. von Neumann, A. & Sprague, R. C. "Hyperactive Children: A continuous long-term placebo controlled follow-up." *JAMA*, 229: 316-317, 1974).

DIETARY INTERVENTION

Dr. Feingold has recently suggested that the occurrence of hyperkinesis and learning disabilities in school age children, irritability, sleeplessness, restlessness and crying in young children and colic in infants, are linked to the ingestion of artificial food colors and flavors. In testimony before the Senate Subcommittee on Health, he has indicated, "Following management (of children whose primary complaint was hyperkinesis or MBD) with a diet eliminating all artificial colors and flavors, we again observed the rapid and dramatic responses in about 50% of cases as reported by our earlier patients. Within a few weeks and sometimes within a few days, a complete reversal of the behavioral pattern was observed."

It must be recognized that the Feingold treatment constitutes more than just the elimination of food colors and food flavors from the diet. In this regard, it should be stressed that:

1) Any diet provides a general nutritional change for the person following the diet.

2) Any treatment intervention initiated to help the patient carries with it definite expectations on the part of the healer and on the part of the patient that improvement will follow from treatment. Non-specific therapeutic improvement (placebo response) is usually observed by the physician, parent, and patient. The Feingold regimen requires a marked change in the family diet and consequently a change in the social interaction of the entire family with the hyperactive child. Thus, fairly strong non-specific

therapeutic changes would be anticipated.

3) Finally, if the Feingold diet eliminates artificial food colors and flavors, then this specific aspect of the diet may be responsible for any observed therapeutic improvement. It should be emphasized that this attribution of specific therapeutic improvement to the elimination of food colors and flavors constitutes only one aspect of the "Feingold" hypothesis. The reason for this emphasis stems from the design implications that follow from the hypothesis that is to be tested. Thus, to test the Feingold regimen implies a test of the general therapeutic change that follows from an admixture of the three components of the regimen that have been elucidated above, i.e., general nutritional changes, altered family social interactions, and the elimination of artificial food flavors and food colors.

In many respects, Dr. Feingold has conceptualized his hypothesis of an adverse behavioral response associated with artificial food flavors and colors as an age-continuum in sensitive children.

For example, he implicated food flavors in the vitamin drops of infants as responsible for the development of colic, and food colors and flavors in the 1-3 year age group as associated with crying, sleeplessness, motor restlessness and irritability. In school age children he implicates the presence of artificial food colors as underlying the behavioral syndrome which is frequently diagnosed as minimal brain dysfuncton or the hyperkinetic reaction of childhood and which includes such symptoms as poor attention span, distractability, hyperactivity, irritability and specific learning disability.

The hyperkinetic syndrome is most frequently diagnosed during the early school years when the task demands placed upon the child in the classroom are most likely to magnify the core symptoms of the disorder, i.e., the inability to sustain attention and to inhibit motor activity. In retrospect, however, these children are typically described by their parents as being "difficult" children prior to coming of school age, i.e., characterized by crying, irritiability, excessive motor activity and emotional lability.

Looking forward in time from the early grammar school period, it seems clear that these hyperkinetic children are at greater risk for academic failure with associated patterns of "acting-out," being loners, emotionally immature, etc. (Weiss, B. Minde, R., Wery, J., Douglas, V. Nemeth, E., Studies on the hyperactive child, VIII, Five Year follow-up. Arch. Can. Psychiat. 24 1971). In all of this process, it is difficult to tease out the behaviors which may stem from initial nutritional causes from the behaviors which may stem from the typical kinds of destructive social interactions that these initial behaviors are likely to call forth from the child's parents, siblings, peers and teachers.

For example, the child who keeps his parents up all night is probably going to be treated somewhat differently than the child who places less of a strain on the emotional and physical resources of his parents. The child who is continually in motion is more apt to find himself in confrontation with his siblings and his peers. The child in school who cannot sit still at his desk and do his school work without being a constant disruption to his classmates and his teacher is much more likely to be labeled as a "trouble-maker" and to develop and internalize a poor sense of personal worth than the child who is not so handicapped. The child who is incapable of sustained attention, despite an adequate IQ, is apt to experience continuous academic failure and is likely to develop a poor self-image. Such a child may turn to delinquent and/or sociopathic behaviors as a result of this labeling process, partly imposed by others and partly internalized as a result of his continuing experience of failing to measure up to his own expectations.

In essence, then, if some children, for whatever reasons, have an intolerance to certain dietary components, it is altogether possible that the symptoms of that intolerance may be manifested differently in different children, given the obvious overlay and interplay of psychosocial factors, personality factors and factors stemming directly from the severity of dietary intolerances or more general nutritional deficiencies.

In order to test the possible etiological relationship between food colors and food flavors and the various manifestations of the hyperkinetic reaction of childhood at different ages, it becomes most important to implement studies using different age groups of behaviorally impaired children who seemingly evidence a therapeutic response to the Kaiser-Permanente (K-P) regimen. By examining different, but age-appropriate components of the hyperkinetic reaction of childhood in relation to nutrition and/or nutritional intolerance, it becomes possible to provide a more theoretically meaningful test of a longitudinal theory that may provide a causal understanding of the development of the hyperkinetic-behavior syndrome in at least some children with this very common behavior disorder of childhood.

REVIEW OF COMPLETED RESEARCH RELEVANT TO THE FEINGOLD HYPOTHESIS

Drawing from his clinical experience, Dr. Feingold has estimated that somewhere between 25-50% of children thought to be hyperkinetic evidence a dramatic therapeutic response to a special diet he has published which eliminates certain artificial food colors and flavors. This material comprises clinical observations and summaries of impressions from his patients and their personal milieu--parents, peers, and teachers. Among the observations are:

(1) the effect of dietary change on a variety of behavior disorders and on patients ranging in age from infants to adults;

(2) the equal therapeutic effect of the diet on children who fail to respond to stimulant medication and those who are responsive to stimulants;

(3) the purported ability of the diet to affect two aspects common to hyperkinesis; learning disabilities and behavioral impulsivity;

(4) the apparently short latency period between a single infraction of the K-P diet, and the expression of behavioral dysfunction.

However, these reports do not constitute a scientific basis for determining the validity of the "Feingold" hypothesis. His writings describe the immense impact of dietary alteration upon the psychosocial dimensions of children classified as hyperkinetic. A clear separation of these two variables, change in dietary constituents and concurrent changes in parent-child relations, is required. Although Dr. Feingold maintains that it is the specific change in dietary constituents (artificial colors & flavors) which produces behavioral improvement, he has not attempted to validate his hypothesis by separating these two components.

In one pilot study conducted by Wender, an attempt was made to investigate the effect of the Feingold diet on hyperkinetic children. The report from this study consists largely of impressionistic observations and no data has been presented to permit statistical analysis. Briefly, the study was conducted in two stages: (1) open screening to find from a group of subjects those who responded to the Feingold diet with behavioral improvement as measured by questionnaire and rating scale and (2) challenge of the "responders" with sodium salicylate or placebo. The concentration of the challenge phase of the study on salicylates reflected Dr. Feingold's past emphasis on salicylates.

Six of eleven children demonstrated an initial behavioral improvement. However, the report states that of the responders, five out of six showed a return to pre-diet behavior over the challenge period even though diet was continued. This deterioration of behavior was not related to dosage with placebo or salicylate. It may be interpreted to cast doubt upon the observation of initial improvement. The subjects and their evaluators (parents and teachers) were probably not blind, and first reports of improvement might reflect expectations or imprecise methods of evaluation. In addition, the study design did not sort out psychosocial effects, possible substantive nutritional change, and specific elimination of additives under the K-P diet. Further, the erratic changes in behavior could be ascribed to infractions of the diet by the subjects. This possibility indicates the need for careful records of compliance.

A study by Conner represents an important preliminary attempt to investigate the Feingold hypothesis by a double blind crossover design. A double blind crossover trial involving a control diet and a diet eliminating artificial flavors, colors and natural salicylates (K-P diet) as recommended by Feingold was conducted on 15 children diagnosed in accordance with the American Psychiatric Association's definition of Hyperkinetic Reactions of Childhood. These children were randomly assigned to either the K-P diet followed by a control diet or to the opposite dietary sequence. Efforts were made to insure that neither parents, teachers, nor the investigator knew which diet the children were on during the experiment (double-blind). Efforts were also made to measure dietary compliance and to match the diets in terms of difficulty of preparation. Teachers and parents observed the children using a standardized symptom rating scale to monitor changes in the symptoms of the hyperkinetic syndrome.

Dr. Conner reports a statistically significant difference between the K-P diet and baseline measures on both parent and teacher ratings; no statistically significant difference between the control diet and the baseline measure; and a statistically significant difference between the K-P diet and the control diet based on teacher ratings, but no significant difference between the K-P diet and the control diet based on parent ratings. Clinical judgment ratings by the investigator also showed significant differences between the two treatments.

The investigator concludes that "the K-P diet may reduce hyperkinetic symptoms" but warns that "it would be hazardous at this point to draw too many conclusions from this experiment, given the small size of the sample and the lack of complete consistency in the results. Any thoughtful observer will understand that a major intervention into dietary habits of a family will produce behavioral effects, regardless of the specific diets, a phenomenon well understood in the management of such conditions as juvenile diabetes. The results would have been substantially clarified if it had been possible to have objective measures of function uncontaminated by the psychological factors which are bound to operate in the family-school-child system. At this point, the results point to the need for considerable further investigation."

The only other available study which has been completed is that conducted by Keithly in California in collaboration with Dr. Feingold. Nineteen hyperactive children were placed on the K-P diet for a period of two to three months. Parents and teachers completed a behavior checklist before the study began and at three-week intervals. Results revealed that parents' evaluations yielded significant gains in the pre-test compared to post-test population means. Notably, evaluations by teachers did not demonstrate significant changes. However, the validity of these findings is questionable in view of the lack of adequate control for dietary intervention and particularly the introduction of numerous biases. The biases occurred by exposing the parents and children to the anticipated outcome of the study before it began, by rewarding children for staying on the diet, and by sending a letter of information to the teachers reflecting what beneficial effects may occur.

In specific terms of either proving or disproving the Feingold hypothesis, the limitations of the available studies conducted to date make them inconclusive. Feingold's original observations are anecdotal and not scientifically controlled or objective. None of the previous studies separated psychosocial changes from dietary intervention, did not adequately "blind" the evaluators, and did not differentiate nutritional change from specific elimination of certain food additives. The data from this last report are questionable primarily because of the biases introduced into the study.

A study at the University of Wisconsin which is currently underway and which will be completed in December, 1975, will provide data on a sample of 45 hyperactive children who participated in an eight-week trial (following a two-week period of baseline evaluation) contrasting the K-P diet with a control diet which includes the average amount of artificial food colors and flavors. A counterbalanced crossover design is employed and an extensive evaluation battery, including parent - teacher blind observer ratings, as well as objective attentional and learning tasks, was employed to assess therapeutic change.

These studies which have been reviewed to date have been of value in indicating the potential difficulties in testing the hypothesis. Statistical analysis becomes especially difficult since the small sample sizes have reduced the significance of all findings. Records of compliance are necessary, and this need raises questions as to whether or not well-controlled outpatient studies can be accomplished. The identification of "responders" is not sufficient if blindedness is not preserved; no "challenge" study has incorporated artificial food flavors and colors to test specificity of responsiveness. Crossover designs may be confounded by loss of blindedness, and disturbing sequence effects should be investigated by either intensive designs using repeated crossovers and/or incorporation of a return to baseline after completion of each diet sequence.

MINIMUM DESIGN REQUIREMENTS FOR A DIETARY STUDY

Before proceeding to a more specific discussion of the issues involved in testing the Feingold diet/regimen, it is useful to examine the relevant criteria advanced by Sprague and Werry (1971) which are as follows:

1) Placebo control

2) Random Assignment of Subjects. Assignment of the subjects to experimental conditions should not depend upon the hunches or other idiosyncratic procedures of a particular investigator for this may seriously bias the sample. If, as is true in many cases in this review, some type of match-pair design is used, then the members of the pairs should be assigned at random to the conditions. If some type of crossover design (a common term in psychopharmacology that indicates a design in which each subject receives each experimental treatment) is utilized, then the subjects should be randomly assigned to the sequences of treatment used in the experiment. Furthermore, random assignment is necessary to meet the minimum assumptions of the statistical tests which should be used to evaluate the findings.

3) Double-blind (DB). This term simply means that neither the subject taking the medication nor the person evaluating the subject's behavior are aware of which is the placebo condition and which is the active medication condition. This procedure attempts to prevent the investigator's expectations from influencing his assessment of the subject's behavior, as well

as the subject's expectations.

4) Standardized Evaluations. By the term "standardized evaluation," it is meant that the measurement instrument has been used before and some empirical information on basic reliability (does the instrument give the same finding when repeated across testers and/or time) and validity (some independent evidence that the instrument is actually measuring what it purports to measure) is available. In addition, it is obvious that more rapid advance can be made if the measuring instrument is anchored in some good theory. (Standardized evaluations are given in the "Special Children's Issue" of the Psychopharmacology Bulletin; 1973).

5) Appropriate Statistical Analysis. It is not sufficient simply to list percentage figures about the degree of improvement in a drug or diet study. Such data are next to impossible to interpret operationally and are seldom subject to scientifically valid tests of replicability. The most acceptable manner of data evaluation is to use some kind of inferential statistical analysis. Mere use of statistics is, however, not sufficient, for they can be and are often grossly abused. An appropriate statistical analysis which does not violate the assumptions of the test used is necessary.

To these criteria, one might add the following additional considerations:

6) Careful Selection and Specification of the Patient Sample. The hyperkinetic child syndrome is difficult to define. It is

currently held that children so diagnosed are heterogenous with respect to possible etiologies and with regard to the specific constellation of symptoms and signs that are commonly accepted as comprising the disorder. Nevertheless, there is general agreement that this syndrome typically includes only children of low normal or higher IQ, without gross physical or neurological handicaps and who are not autistic, schizophrenic, primarily asocial, aggressive, or overanxious. Situational stress reactions are usually excluded by requiring a history of the disorder of a few years and by requiring that the child be perceived as trans-situationally hyperactive (i.e., judged as hyperactive by at least two classes of observers such as parents and teachers, parents and physicians, teachers and physicians). It may also be helpful to require a minimum severity score on the target symptoms of hyperactivity. Many investigators have employed this procedure and have required a score of at least 15 out of a total possible score of 30 on the hyperactivity factor of the Conner's Teachers Questionnaire (Conners, C.K., A teacher rating scale for use in drug studies with children. Amer. J. Psychiat., 126:152-156, 1969). Each subject should receive a physical examination to detect overt nutritional deficiency symptoms and an analysis of blood for iron, zinc, lead, ferritin, and RBC folate. In addition, a fasting blood glucose and a urinalysis for nicotinic acid should be accomplished. History of allergy involvement should be obtained by interview and, where available, medical records. Unless evidence is obtained for existence of allergies, no testing is recommended. Random selection is required among subjects having values for any parameters found to deviate from normal ranges.

Standardized neurological exams and phychological tests are frequently employed to document the presence of attentional deficits, distractability, poor coordination, soft neurological signs, and so forth.

If a non-hyperactive learning disability subgroup is to be included, it is considered desirable to require at least one year of retardation in reading and/or arithmetic on a standard test of achievement such as the Peabody Achievement Test.

Characterization of the study sample with regard to possible etiology as well as with regard to parameters of CNS functioning such as level of cortical arousal may also be desirable because of the heterogeneity of the group of children who are characterized as hyperactive, MBD, learning disorders, etc.

The sample should also be characterized with regard to social class, family integration, and other types of previous therapy, such as pharmacotherapy, family counseling, tutoring, special education, and behavior modification. Detailed information should be collected on eating habits and a careful dietary history should be taken on all children. These data might provide new important predictor information for understanding the subgroup of children who evidence maximal therapeutic improvement. Thus, for example, by regressing scores representing the adequacy of the child's eating habits and prior nutritional intake against improvement in symptomatology (associated with the K-P diet and/or the control diet), it becomes possible to determine the extent to which prior dietary adequacy may modify the the magnitude of the therapeutic response to the dietary intervention. If general nutritional factors played an etiological role in hyperkinesis, one would expect reliably more improvement in those children who initially had histories of poor eating habits and nutritionally impoverished diets.

7) Adequate Baseline Observations. Since many rating instruments are characterized by "practice" effects and since many hyperkinetic children are on treatment regimens which may have to be terminated in order to make them eligible for dietary study protocols, it is very important that adequate baseline periods be employed to allow for pretreatment stability of target symptoms.

8) Dietary Specification and Evaluation with Regard to: a) general nutritional adequacy: b) compliance with dietary specifications

in terms of both inclusions and exclusions. It should be realized that to the extent that children deviate from the K-P diet (which contains no artificial food colors or food flavors) the likelihood of finding support for the efficacy of the K-P diet is diminished. For this reason, an inpatient setting which would provide the opportunity for very close supervision of food intake would seem desirable. When obvious dietary violations occur, whether in an inpatient or outpatient trial, the data from that patient (whether on the control or K-P diet) should be excluded from all data analyses. Whatever the diet the child is given, K-P or "control," actual food intake should be carefully specified and closely monitored.

For an individual child, 5- or 7-day records are considered adequate for determining intakes of the major nutrients such as carbohydrate or protein. Twenty-four hour recalls are considered inadequate to assess nutrient intakes of groups of children. The number of children needed to obtain valid information from 24-hour recalls, under a variety of circumstances, has never been very well defined. Because of the variability of intake of trace nutrients, food additives, or contaminants and the requirement for accurate and precise knowledge of intake, it is recommended that three continuous weeks of records of food intake be obtained for each child.

Analysis of foods should include iron, zinc, lead, and color additives, if possible. Estimation of dietary fat, protein, carbohydrates, tyrosine, and tryptophan shall be calculated from dietary intake using table values.

In order to maximize the likelihood of dietary compliance, the entire family should follow the diet prescribed for the child. Further, it would seem prudent for the research team to provide the food for the complete diet to the entire family for the full duration of the clinical trial.

The control diet should provide levels of all nutrients equal to those established by the Recommended Dietary Allowances of the National Academy of Sciences.

The National Advisory Committee on Hyperkinesis and Food Additives in their report to the Nutrition Foundation (June 1, 1975) were so concerned with a true double-blind testing of the K-P diet that they state, " ... in a home setting there be used but one diet, i.e., no "control diets," because of anticipated difficulty in assuring compliance and the impossibility of avoiding the placebo effect."

They indicate further, "... the utilization of alternative dietary plans, i.e., the K-P diet and a "control," even when randomly administered, precludes strict double-blind testing and introduces the variable placebo effect."

9) Multiple Outcome Criteria. Whenever possible, it is suggested that a variety of raters and a variety of different types of outcome criteria be included to evaluate therapeutic response. Thus, types of raters might include (a) parents; (b) teachers; (c) school peers; (d) clinicians; and (e) trained observers independent of the study *per se*. Elements of rating might include: (a) attentional tasks; (b) learning tasks (such as paired-associate learning, recognition, mazes, etc.); (c) objective measures of activity such as actometers, stabilimetric cushions, grid crossing, etc; (d) subjective estimates of behavioral change in activity level, distractability, impulsivity, ability to sustain attention, sociability, and so on, by the different types of raters indicated above.

10) Study Duration. Most treatment regimens for the hyperkinetic child syndrome are administered over extended periods of time, e.g., years. While typically the initial treatment efficacy of a particular regimen is established in the context of a short-term treatment protocol, e.g., a few months, it ultimately becomes most important to encourage and support the collection of long-term efficacy and safety data. The early recognition and public health commitment to this stratagem is particularly important when dealing with the still developing child. The possibility of late onset of adverse effects, stemming from a treatment with an established short-term efficacy and safety record, must not be overlooked. Naturally, this consideration

only becomes of concern if short-term efficacy and safety are firmly established. The prudent investigator should consider the necessary logistics for the long-term followup of study cohorts and should plan for a six-month or twelve-month followup to obtain some information with regard to whether or not the prescribed study diet is still being followed and how the child is doing at home and at school.

11) Sample Size. The sample size necessary to demonstrate a statistically significant difference between two relevant regimens depends upon the "true" magnitude of treatment differences and upon the magnitude of sources contributing to subject variability and errors of measurement. Preliminary projections based upon pilot data suggest that a study population of between 30 and 60 should be required to be fairly certain of detecting a 20 percent difference in response between the K-P regimen and a control regimen. The above projection is based on a crossover design and roughly twice this sample size (70-100 children) would be required to obtain this same degree of sensitivity in an independent group design.

MODEL DESIGNS

Model Design A

To determine whether there is any therapeutic benefit to be derived from any aspect of the Feingold dietary regimen (general nutritional component + psychosocial changes in the family interactions + specific elimination of artifical food colors and food flavors), one might identify a suitable group of children diagnosed as having the hyperkinetic reaction of childhood and randomly assign half the sample to a treatment waiting list (for ethical reasons only a few weeks should be used) while the other half of the sample received the Feingold diet. Pre- and post-treatment evaluations on an appropriate battery of therapeutic outcome measures and tests would provide an overall evaluation of the Feingold regimen. Some information regarding the importance of the general nutritional component of the Feingold regimen might be obtained by taking a careful dietary history of all children assigned to the study and examining the magnitude of therapeutic improvement on the Feingold regimen against the prior nutritional adequacy of the child's diet. If those children who were judged initially to have the least adequate diets evidenced the most improvement on the Feingold regimen, this relationship would be suggestive of a general therapeutic benefit from the non-specific nutritional component of the K-P diet.

Issues of dietary compliance are of considerable importance in evaluating the results of data generated from studies employing this type of design.

Since it is rather generally accepted that any dramatic psychosocial and/or quasi-medical intervention is likely to result in at least some therapeutic benefit, this Model Design A does not seem particularly relevant except insofar as it may cast some light on issues related to a possible association between nutrition and behavior.

Model Design B

The Blue Ribbon Panel (see appendix) made the point that hyperkinesis may be associated with hunger and it seems clear that behavioral disorders may also be associated with nutritional deficiencies of various kinds.

In order to determine the general nutritional benefit of various diets, including the Feingold regimen, it must be possible to develop an appropriately large sample of children with the hyperkinetic syndrome and randomly assign them to either the K-P diet or another diet, judged by a group of nutritional experts to be nutritionally adequate. In order to equalize "placebo effects" the control diet should involve the same degree of dietary difficulty for preparation as the K-P diet. This design might proceed as an independent group design (no crossover) or as a counter-balanced crossover design in which the sequence of diets was randomized.

Issues with regard to dietary compliance and with regard to the double-blind condition of the study will require careful monitoring. In this regard it would be helpful for potential investigators in this area to develop standardized procedures and questionnaires to tap these important concerns prior to the initiation of studies with this type of design because of the difficulty in maintaining the double-blind.

It must be stressed that Model Design B provides information with regard to general dietary response and not with regard to specific dietary additives per se.

Model Design B is not as straightforward as Model Design C (vide infra) and is open to more possible sources of bias with regard to the potential breaking of the double-blind and issues around dietary compliance. It does address the broader public health concern of general nutritional factors and their possible etiological significance for the symptoms of the hyperactive child syndrome. It also provides some opportunity to examine the more specific Feingold hypothesis but in a less direct fashion than does Model Design C.

It must be recognized that "diet" represents a most complex independent variable in that two diets may differ along many nutritional dimensions so that finding a therapeutic advantage (or disadvantage) for the K-P diet vs. the control diet would not enable the researcher to conclude that the differences between the diets was necessarily attributable to the presence or absence of artificial food colors and food flavors.

Model Design C

The most direct test of the Feingold hypothesis is one in which the children who have responded to his diet be maintained on the same treatment regimen plus the addition, in a double-blind fashion, of chocolate cookies, candy, or other food items prepared in such a fashion that one-half of the items will contain no food additives and the other half will contain the eight more common food additives at levels calculated to average what a child on an ordinary diet might take in daily.

The selection of challenge components and/or factors should be prioritized according to the distribution and relative concentration of suspect materials in the food supply. Consideration should also be given to the scientific evidence that might support the selection of particular compounds.

Levels of challenge materials to be used in the diet shall be established by estimating the levels normally found in foods. The use of quantities above the levels normally found in food should only be sanctioned where safety is assured and where additional amounts will provide some beneficial effect.

Given this general model one could use either an (a) "independent" group design (if the sample size was sufficiently large) with children randomly assigned to the "pure" K-P diet or the K-P "challenge" diet; (b) a counterbalanced crossover design in which each child serves as his own control and is randomly assigned to either the "pure" to "challenge" sequence or the "challenge" to "pure" sequence (fewer children would be needed to achieve the same degree of statistical power as compared with the "independent" group designs); or (c) a multiple crossover design such as proposed by Dr. Chassan (see Principals and Problems in Establishing the Efficacy of Psychotropic Agents, (Eds.) Levine, Schiele, and Bouthilet, 1971) and has come to be called the "intensive" design. It should be noted that the "intensive" design provides for sufficient crossover data points to permit the statistical evaluation of dietary effects for each child included in the study. All variants of the Model Design "C" permit a direct test of the specific Feingold hypothesis that artificial food flavors and colors (or whatever constituents are put into the challenge chocolate bar) are directly associated with adverse behavioral effects, such as hyperactivity, poor attention span, distractability, irritability, etc.

This type of design does not provide a general test of the K-P regimen insofar as that regimen may be nutritionally superior to the child's previous nutritional intake or insofar as the K-P regimen is likely to provide the child with a generally more therapeutic type of interaction with other members of the family. Should the results of this type of study design prove positive; i.e., children receiving the food color-flavor additives show statistically significant deleterious effects relative to the pure K-P dietary condition, then by the process of eliminating different constituents of the challenge, it would be possible to pinpoint the particular dietary offenders either on a group basis or on an individual basis, if an intensive design was employed.

The possible mechanisms of action might also be explored if it was firmly established that the Feingold hypothesis was indeed correct. Should the results of studies conducted with Model Design "C" prove negative, one might then make a decision with regard to the public health significance of evaluating the other aspects (general nutritional components and psychosocial components) of the Feingold regimen. From a scientific perspective, this design is clearly superior to other possible designs in terms of preserving the double-blind. The preservation of the double-blind is, of course, most critical to the subjective interpretations of therapeutic change made by parents, teachers, and members of the treatment team.

Since Dr. Feingold has claimed that only from 30 percent to 50 percent of hyperkinetic children show improvement on the K-P diet, the ICGH strongly recommends that children be pretested on the K-P diet in an open pre-study phase and that only those children who show a "good" response to the K-P regimen be entered into the more formal (i.e., double-blind) study design. It was also suggested that washout periods be inserted between the K-P diet and the K-P challenge diet (to control for possible pharmacologic carryover effects) and that an A-B-A vs B-A-B sequence be employed to avoid the potential statistical problems in an A-B vs B-A crossover design in which a sequence by treatment interaction can cloud the interpretation of pooled treatment differences.

Model B and C Combined

One interesting variant of the designs discussed above is the possibility of combining aspects of Model Design B with Model Design C. Thus, for example, one could start with a pool of carefully diagnosed hyperkinetic children who were randomly assigned to either the K-P diet or a nutritionally adequate control diet which contained artificial food colors and food flavors (Model Design C). After an appropriate dietary trial of four weeks on each diet, using a cross-over design, those children showing a favorable therapeutic response to the K-P diet but not to the control diet would enter a Model Design C Study, i.e., K-P vs. K-P challenge in a counter-balanced, double-blind, crossover sequence.

The initial phase of this study would provide information about dietary response (Model Design B) whereas the second phase of the design (Model Design C) would provide more specific information about the role of food colors and food flavors. One advantage for this combination Design is that it would cast light on both the percentage of hyperkinetic children who were responsive to general dietary regimens as well as to the more specific aspects of the K-P dietary regimen.

SUMMARY

The Interagency Collaborative Group on Hyperkinesis has held five formal meetings and numerous informal meetings over the past three months in order to carry out its assignment.

One of these meetings consisted of an all day conference on hyperkinesis and diet attended by scientists from several universities and representatives from the legal profession, press and consumer groups. The Group has directed its efforts toward an exchange of information concerning some of the research issues relevant to hyperkinesis and diet, a review of the appropriate literature, assessment of ongoing or completed research studies, and a review of several proposed studies in order to explore whether or not dietary modification contributes significantly to a reduction of symptoms in children with the hyperkinetic syndrome.

The clinical definition of the hyperkinetic syndrome typically excludes children of less than low normal intelligence. The major symptoms of the hyperkinetic syndrome are an increase of purposeless physical activity and a significantly impaired span of focused attention. The child is easily distracted, racing from one idea or interest to another.

The diagnosis is clearly best made by a skilled observer and, unfortunately, there is no single diagnostic test. As a result of diagnostic difficulties, crude estimates of the prevalence of the hyperkinetic syndrome vary considerably. One conservative estimate is that 3 out of 100 elementary school children have moderate to severe behavioral disorders. However, a five-fold range in estimates of prevalence made it impossible to determine the true number of children showing behavior patterns associated with hyperkinesis.

Although many factors seemed to be involved in the etiology of the hyperkinetic behavioral syndrome, specific factors have been implicated in some individual cases.

The Group reviewed some of the observed relationships between the occurrence of the hyperkinetic syndrome in children and such factors as the social environment, biochemical, nutritional status, allergy or intolerance to foods and exposure to toxic substances.

SOCIAL FACTORS:

It would be difficult to over-emphasize the importance of the social environment in discussing the etiology of behavior syndromes in children. Tensions arising from poor social relationships can trigger hyperactive behavior which may contribute to further deterioration of relationships between the child and his parents, teachers and peers. However, caution must be exercised in employing simple explanations of the effects of increased activity on socialization. It has been proposed that moderate to high levels of activity usually go along with social success. Even though a social-behavioral view of hyperkinetic behavior is undoubtedly incomplete, some awareness of social factors is necessary in considering etiology and in making treatment plans for the hyperkinetic child.

NUTRITIONAL STATUS:

One of the ways diet may have effects on behavior is by modifying the biochemistry of the nervous system. Alterations in the quality, quantity, and timing of intake of food ingredients can involve changes which may affect the body's metabolism and the function of various organs, including the brain. Deficiencies of nutritionally required ingredients such as vitamins are one potentially relevant mechanism.

Some cases of the hyperkinetic syndrome have been linked etiologically to hypoglycemia (low glucose availability). In such individuals who are susceptible to reactive (post absorptive) hypoglycemia, the relative proportions of energy yielding nutrients available to the central nervous system can affect the occurrence of symptoms.

ALLERGY, INTOLERANCE, AND TOXICITY:

It has recently been suggested that the occurrence of hyperkinesis and learning disabilities in children, and of sleeplessness, irritability and colic in infants, is linked to the ingestion of artificial food colors and flavors in foods. A diet free of these food additives has been advocated by some individuals as a means of reducing the symptom level of children with the hyperkinetic-behavior syndrome. A limited number of research studies have attempted to verify this hypothesis.

CONCLUSIONS:

The Group has reviewed the available data and information from those dietary studies which have been completed and made available for review. All of these studies have methodological problems consisting of small study populations, difficulties in maintaining a "blind" component in the use of diet, difficulty in imposing dietary restrictions and questions concerning data analysis.

Only when the children, parents, and evaluators of behavioral changes are unaware of which diet is being ingested by the children studied can biases based on hope and expectations of improvement in behavior be avoided.

It is the opinion of the Group that these studies have neither proven nor disproven the hypothesis that a diet free of artificial food colors and flavors reduces the symptoms in a significant number of children with the hyperkinetic-behavior syndrome. The Group feels, however, that the evidence taken as a whole is sufficient to merit further investigation into the relationship of diet and the hyperkinetic syndrome.

RECOMMENDATIONS:

The Group urges that basic behavioral, neurophysiological, and biochemical research in the area of hyperkinesis receive continued support. The possibility that fundamental neurochemical abnormalities underlie many of the manifestations of hyperkinetic behavior is a real one, and the research efforts needed to find these answers are broader than just those discussed in this report.

The Group recognizes that a valid assessment of the Feingold dietary regimen must be designed to test the general therapeutic change that may follow from a mixture of the three components of the regimen, i.e., general nutritional changes, altered social interactions and the elimination of artificial food flavors and colors with the separation and assessment of these components to be carried on in an age-continuum of infants, and 1-5 and 6-12 year old children.

The Group is aware that one study presently underway will be completed as of early December and the data analyzed for presentation and review by early 1976. The Group believes that further study with these children should be performed if feasible. Such a study (Model C) would involve testing the children responsive to the K-P diet with food preparations having quantities of artificial food colors and/or flavors consistent with average dietary intakes.

The Group also believes it important to perform another efficacy study of the dietary regimen in an outpatient population (Model B), to be followed by a challenge (Model C) type study on the same population's responders to the K-P diet.

Of additional current importance would be a study to explore whether or not infants with colic, or young children who show high levels of irritability, fidgetiness, sleeplessness and crying, exhibit such behavioral characteristics as a result of intolerance to artifical food colors and/or flavors.

If the studies above demonstrate positive results supporting the efficacy of the K-P dietary regimen in reducing the symptoms of children with the hyperkinesis syndrome, it then becomes a more complex problem to define the etiologic factors and mechanisms involved.

APPENDIX A

REPORT

OF THE CONFERENCE ON THE USE OF STIMULANT DRUGS IN THE TREATMENT OF BEHAVIORALLY DISTURBED YOUNG SCHOOL CHILDREN

Sponsored by the Office of Child Development and
the Office of the Assistant Secretary for Health and Scientific Affairs
Department of Health, Education and Welfare
Washington, D.C., January 11-12, 1971

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Introduction

On January 11-12, 1971, the Office of Child Development and the Office of the Assistant Secretary for Health and Scientific Affairs, Department of Health, Education, and Welfare, called a conference to discuss the use of stimulant medications in the treatment of elementary school-age children with certain behavioral disturbances. In convening the conference, the Office of Child Development was aware of public concern about the increasing use of stimulant medications (such as dextroamphetamine and methylphenidate) in treating so-called hyperkinetic behavior disorders. Were these drugs--so widely misused or abused by adolescents and adults--truly safe for children? Were they properly prescribed, or were they used for youngsters who, in fact, need other types of treatment? Is emphasis on medications for behavior disorders misleading? Might this approach tempt many to oversimplify a complex problem, leading to neglect of remedial social, educational or psychological efforts on the part of professionals, parents, schools and public agencies?

In order to clarify the conditions in which these medications are beneficial or harmful to children, to assess the status of current knowledge, and to determine the best auspices for administering these drugs to children, a panel of fifteen specialists was invited to meet in Washington. The panelists were from the fields of education, psychology, special education, pediatrics, adult and child psychiatry, psychoanalysis, basic and clinical pharmacology, internal medicine, drug abuse and social work. The panel's task was to review the evidence of research and experience and to prepare an advisory report for professionals and the public.

This report briefly outlines the general nature of behavioral disorders in children and then focuses on those disorders that are being treated with stimulant medications. It discusses appropriate treatment and the concerns voiced by the public and media. Finally, the report examines the role of the pharmaceutical industry, professionals, and the news media in publicizing stimulant drugs for children and outlines the glaring gaps in needed research, training and facilities.

Behavior Disorders of Childhood

A wide range of conditions and disabilities can interfere with a child's learning at home and in school, his socialization with peers, and his capacity to reach his maximum development. Social deprivations and stress at home or school may retard optimal development. Mental retardation, the more rarely occurring childhood autism and psychosis, and other such disabilities may cause serious problems. Some difficulties arise because of clearly definable medical conditions such as blindness, deafness or obvious brain dysfunction. Some are associated with specific reading or perceptual defects, and others with severe personality or emotional disturbance.

Such dysfunctions are known to require careful evaluation, thoughtfully planned treatment employing a variety of methods on the child's behalf, and conscientious monitoring of remedial treatments. Individualized evaluation and treatment is important for any childhood behavior disorder. There are appropriate occasions for use of medications such as tranquilizers and anti-depressants in some children with these disorders. For over three decades, stimulant medications have been selectively used for children under medical supervision. We now focus upon issues related to the current use of these drugs.

"Hyperkinetic Disorders"

The type of disturbance which has evoked misunderstanding and concern has many names. The two most familiar--neither entirely satisfactory--are "minimal brain dysfunction" or, more commonly, "hyperkinetic behavioral disturbance." There is no known single cause or simple answer for such problems. The major symptoms are an increase of purposeless physical activity and a significantly impaired span of focused attention. The inability to control physical motion and attention may generate other consequences, such as disturbed mood and behavior within the home, at play with peers, and in the schoolroom.

In its clear-cut form the overt hyperactivity is not simply a matter of degree but of quality. The physical activity appears driven--as if there were an "inner tornado"--so that the activity is beyond the child's control, as compared to other children. The child is distracted, racing from one idea and interest to another, but unable to focus attention.

Incidence of Hyperkinetic Disorders

This syndrome is found in childrenof all socioeconomic groups and in countries throughout the world. A conservative estimate would be that moderate and severe disorders are found in about 3 out of 100 elementary school children--an estimate that would vary somewhat in different communities. More males than females are affected, as is true in a number of childhood ailments. Children so afflicted are generally of normal or superior intelligence. A significant number so diagnosed have special learning or reading disabilities, in addition to the major sypmtoms. A near majority are reported to have had behavioral problems since infancy. There is a smaller group of more severely afflicted children upon whom most studies have focused; they may show increased clumsiness and a variety of physical symptoms. Thus, some of the children show hyperactivity and reduced attention which ranges in degree from mild to severe, with or without associated physical signs or special learning impairments; some have complex behavioral and personality problems, as well as special learning and reading difficulties, along with the major hyperkinetic symptoms.

Causes of Hyperkinetic Disorders

We know little about definitive causes. The disorder has been ascribed to biological, psychological, social or environmental factors, or a combination of these. There is speculation that the core set of symptoms--those affecting control of attention and motor activity--may have their origin in events taking place before the child is born, or during the birth process, or they may be related to some infection or injury in early life. The neurological and psychological control of attention is an important but incompletely researched topic, as are the nutritional, perinatal and developmental factors. Thus, in many instances, it is not yet possible even to speculate as to original causes.

The Course of Hyperkinetic Disorders

Usually, the excessive activity and attentional disturbances are less apparent after puberty. Specialists citing experience and some fragmentary research data believe that treatment enables many to lead productive lives as adults, while severely afflicted children who remain untreated may be significantly at risk for adult disorders. Extensive research is still required on these points. Because the ages of 5 to 12 are crucial to the child's development and self-image, treatments which permit the child to be more accessible to environmental resources are warranted and useful.

Diagnosis of Hyperkinetic Disorders

In diagnosing hyperkinetic behavioral disturbance, it is important to note that similar behavioral symptoms may be due to other illnesses or to relatively simple causes. Essentially healthy children may have difficulty maintaining attention and motor control because of a period of stress in school or at home. It is important to recognize the child whose inattention and restlessness may be caused by hunger, poor teaching, overcrowded classrooms, or lack of understanding by teachers or parents. Frustrated adults reacting to a child who does not meet their standards can exaggerate the significance of occasional inattention or restlessness. Above all, the normal ebullience of childhood should not be confused with the very special problems of the child with hyperkinetic behavioral disorders.

The diagnosis is clearly best made by a skilled observer. There unfortunately is no single diagnostic test. Accordingly, the specialist must comprehensively evaluate the child and assess the significance of a variety of symptoms. He considers causal and contributory factors--both permanent and temporary--such as environmental stress. He distinguishes special dysfunctions such as certain epilepsies, schizophrenia, depression or anxiety, mental retardation or perceptual deficiencies. The less severe and dramatic forms of hyperkinetic disorders also require careful evaluation. Adequate diagnosis may require the use not only of medical, but of special psychological, educational and social resources.

Treatment Programs

The fact that these dysfunctions range from mild to severe and have ill-understood causes and outcomes should not obscure the necessity for skilled and special interventions. The majority of the better known diseases--from cancer and diabetes to hypertension--similarly have unknown or multiple causes and consequences. Their early manifestations are often not readily recognizable. Yet useful treatment programs have been developed to alleviate these conditions. Uncertainty as to cause has not prevented tests of the effectiveness of available treatments, while the search for clearer definitions and more effective kinds of therapy continues. The same principles should clearly apply to the hyperkinetic behavior disorders.

Several approaches now appear to be helpful. Special classes and teachers can be directed to specific learning disabilities and thus restore the confidence of the child who experiences chronic failure. Modification of behavior by systematic rewarding of desired actions has been reported to be useful in some children. Elimination of disturbing influences in the family or classroom through counseling may often tip the balance, and a happier child may show improved control and function.

There will be children for who such efforts are not sufficient. Their history and their examination reveal symptoms of such a driven nature that skilled clinicians undertake a trial of medical treatment. Medicine does not "cure" the condition, but the child may become more accessible to educational and counseling efforts. Over the short term and at a critical age, this can provide the help needed for the child's development.

Stimulant medications are beneficial in only about one-half to two-thirds of the cases in which trials of the drugs are warranted. The stimulant drugs are considered to be the first and least complicated of the medicines to be tried. Other medications--the so-called tranquilizers and anti-depressants--are generally reserved for a smaller group of patients. Without specialized medical therapy, the consequences for these children of their failure to manage--even in an optimal environment--are clearly very severe. In such cases, the aim is not to "solve problems with drugs," but to put the severely handicapped child in a position to interact with his environment to the extent that his condition permits.

Response to stimulant medication cannot be predicted in advance. Fortunately, the issue can be resolved quickly. When stimulants are given in adequate doses, a favorable response--when it occurs--is fairly rapidly obtained and is unmistakably the consequence of the drug. Thus, if an adequate test of pharmacotherapy (a few days or weeks) produces only doubtful benefits or none at all, treatment can be promptly terminated. The physician will, of course adjust dosage carefully to assure an adequate therapeutic trial. It would be tragic to deprive a child of a potentially beneficial treatment by inattention to dose. Thus, it is clear that not all affected children require medication and that of those who do, not all respond.

When the medication is effective, the child can modulate and organize his activities in the direction he wishes. The stimulant does not slow down or suppress the hyperkinetic child in the exercise of his initiative. Nor does it "pep him up," make him feel high, overstimulated, or out of touch with his environment. Much has been made of the "paradoxical sedative" effect of stimulants in such children. The term is inappropriate. Although their exact mechanism of action is not known, stimulants do not provide a chemical straitjacket. They do not act as a sedative. Rather, they appear to mobilize and to increase the child's abilities to focus on meaningful stimuli and to organize his bodily movements more purposefully.

The hoped-for secondary consequences are better peer relationships, improved self-image, and pleasure in acquiring competencies. Any coexisting dysfunctions--such as special perceptual and learning handicaps--must not be left unattended, simply because pharmacotherapy is available and sometimes helpful. Similarly, personality and psychological problems, social and family problems, may require continued attention.

During drug treatment, the dosage may require shifting to minimize unwanted effects, of which the major ones are loss of appetite and insomnia. Drug treatment should not and need not be indefinite, and usually is stopped after the age of 11 or 12. Frequently, following a sustained improvement over several months or a year or so, drugs may be discontinued, as during a vacation period. Drug-free intervals can be prolonged as observers assess the child's condition.

The decision to use drug treatment thus depends on the commitment to diagnose and to monitor the response to treatment in the best traditions of medical practice. When there is informed parental consent, parents, teachers and professionals can collaborate in organizing and monitoring treatment programs.

Concerns Raised by the Public and the News Media

We will now turn to various concerns about hazards and abuses when stimulant medications are used for children. For example, concern has been expressed that the medical use of stimulants could create drug dependence in later years or induce toxicity. This subject touches on the rights of the child to needed treatment, as well as risks to both the child and the public, and requires continued intensive scrutiny.

1. Does the medication produce toxicity?

One should not confuse the effects of intravenous stimulants and the high dosages used by drug abusers with the effects or the risks of the low dosages used in medical therapy. In the dosage used for children, the questions of acute or chronic toxicity noted in the stimulant abuser are simply not a critical issue. Unwanted mental or physical effects do rarely appear in children; cessation of therapy or adjustment of dosage quite readily solves the problem.

2. Is there a risk of drug dependency in later years?

Thirty years of clinical experience and several scientific studies have failed to reveal an association between the medical use of stimulants in the pre-adolescent child and later drug abuse. Physicians who care for children treated with stimulants have noted that the children do not experience the pleasurable, subjective effects that would encourage misuse. They observe that most often the child is willing to stop the therapy, which he views as "medicine." Thus, the young child's experience of drug effects under medical management does not seem to induce misuse. The medical supervision may "train" him in the appropriate use of medicines. When adults are given stimulants--or even opiates--for time-limited periods under appropriate supervision and for justifiable reasons, there is relatively little misuse. Similarly, in treating epilepsy, barbiturates have been given from infancy to adulthood without creating problems of dependency or abuse.

It is not ordinarly the drug which constitutes abuse but the way in which a drug and its effects are used and exploited by an individual. There are indeed adolescents who; in varying degrees and for varying periods of time either misuse or dangerously abuse stimulants. They experiment with the effects of excessive dosages to create excitement, to avoid sleep, to defy contraints, and to combat fatigue and gloom. It should be noted that these drugs are not commonly prescribed to children after the age of 11 or 12, when the actual risks of such experimentation or misuse might possibly become more significant.

Alert monitoring of drug use at any age is a part of sensible medical practice. With such precaution and with the available evidence, we find minimal cause for concern that treatment will induce dangerous drug misuse. To the contrary, there are very good reasons to expect that help, rather than harm, will be the result of appropriate treatment.

3. Are there safeguards against misuse?

There are some sensible steps, in addition to medical control, that guard against possible misuse. The child should not be given sole responsibility for taking the medication. He usually need not bring the drug to school. The precautions that surround the medicine cabinet--whether antibiotics, aspirins, sedatives or other medications are present--should be applied. Many such medicines, when misused, can be more dangerous to health and life than even the stimulant drugs. No child in the family should have access to medications not presecribed for him. These are general precautions comprising a part of the child's eduction in the "etiquette of the medicine cabinet."

4. Do stimulants for children create a risk for others?

The panel agrees that stimulant drug abuse is seriously undesirable and frequently dangerous, although views vary on the scope of the problem and the number of actual casualties. Experts also agree that far more stimulants are prescribed for adults than are medically needed and far more are manufactured than prescribed.

Overprescription of any medication is deplored, whether or not it is liable to abuse. The question is whether the availability of stimulants for a very few of the childhood behavior disorders threatens the public health

The prescribed dosage for an individual child constitutes an insufficient quantity to supply the confirmed abuser of stimulants with the amounts he requires. It is also true that illicitly manufactured stimulants are quite readily available and abused in this country. We must weigh the advantages of having appropriate medication available against the dangers of withholding treatment from a child who can clearly benefit from it. We doubt that prescriptions for the children who benefit from stimulants will require the manufacture of excessive and dangerously divertible supplies. With sensible precautions, there is at present no evidence justifying sensational alarm. either about the safety of the individual child who can benefit from therapy or about the safety of the general public.

5. Does medication handicap the child emotionally?

It is sometimes suggested that treated children may not be able to learn normal responses and master adjustments to the stresses of everyday life. These fears are understandable but are not confirmed by specialists who have experience with the conditions and the situations in which medications are properly used. For the correctly diagnosed child, these medications--if they work at all--facilitate the development of the ability to focus attention and to make judgments in directing behavior. Such children can acquire the capacity to tolerate the master stress. The medications, in these circumstances, help "set the stage" for sstisfactory psychological development.

The hyperkinetic behavioral disturbance is a form of diorganization that creats great stress in the afflicted child. The use of therapeutic stimulants for this disturbance should not be equated with the misuse of medication aimed at allowing a normal child or adult to avoid or escape the ordinary stresses of life.

6. What are the rights of the parents?

Under no circumstances should any attempt be made to coerce parents to accept any particular treatment. As with any illness, the child's confidence must be respected. The consent of the patient and his parents or guardian must be obtained for treatment. It is proper for school personnel to inform parents of a child's behavior problems, but members of the school staff should not directly diagnose the hyperkinetic disturbance or prescribe treatment. The school should initiate contact with a physician only with the parents' consent. When the parents do give their approval, cooperation by teachers, social workers, special education and medical personnel can provide valuable help in treating the child's problem.

Stigmatizing the Medicines and Children, and the Role of Public Education

A child who benefits from stimulants or other psychotropic medications should not be stigmatized; his situation is no different from that of the child who benefits from eyeglasses. It is unjust to stigmatize a child in later life, when competing in various situations (applying for college, employment or organization memberships), by labeling him early in life as "stupid" an "emotional cripple," a "drug-taker," or by any other kind of unjustified and unfortunate stereotype.

Nor should the medicine be stigmatized. Where bad practices prevail--and a number of complaints have been called to our attention--these practices should be squarely dealt with. This is not only a responsibility of physicians and educators, but also of the news media. Yet indignation must be tempered with perspective and scrupulous respect for the facts. An informed and understanding public can foster the growth and development of children, and these public attitudes may lead to the development of more refined and better-delivered health services. Either bad practices or exaggerated alarm can threaten the availability of medical resources for those who critically need it. This has happened before in the history of valuable medicines and it can take years to repair the damage.

The Promotion of Drugs by Industry and the Media

Pharmaceutical companies producing stimulants or new medications which may become useful for hyperkinetic disorders have a serious obligation to the public. These medicines should be promoted ethically and only through medical channels. Manufacturers should not seek endorsement of their products by school personnel. In the current climate, society can best be served if industry refrains from any implicit urging that nonspecialists deal with disorders and medications with which they are unfamiliar. Professionls and the news media can play useful roles by not pressing for treatments in advance of their practical availability.

The Delivery of Special Health Care: A Dilemma

Our society has not as yet found complete solutions to the problem of the delivery of special health care. When available treatments cannot be confidently and appropriately delivered by physicians, they are perhaps best withheld until such treatments can be provided--especially with milder dysfunctions. This is not to say that severly afflicted hyperkinetic children should not or cannot receive available medical treatment. But until systems of continuing professional education and ready access to consultants are financed and perfected, some judgment about the pace at which unfamiliar treatments can be widely fostered is required. Finally, we must recognize that it is not only the scarcity of trained personnel, but factors such as poverty and inadequate education facilities which prevent accessibility to individualized treatment.

The Need for Skills and Knowledge

In preparing this report, the Committee was repeatedly struck by our lack of information in many crucial areas. The facts are that children constitute well over half our population, but receive a disproportionately low share of skilled research attention. We have noted the difficulties in arriving at accurate methods of diagnosis and the importance of launching careful longitudinal and follow-up studies. The investigation of causal factors lags. Such factors as perinatal injury, environmental stress or the development of the neurological and psychological controls of attention require study. Variations in different socioeconomic and ethnic groups must be considered in order to arrive at better definitions of behavior properly regarded as pathological. All such research efforts would have aided us in assessing the numbers of affected children and in recommending designs for more effective treatment programs.

Clinical pharmacologists have repeatedly found that drugs may act differently in children than in adults. To use medicines of all kinds effectively in children, more specialists must be trained in drug investigation--pharmacologists who can develop basic knowledge about the action of drugs in the developing organism. There is the obvious need for better and more precisely targeted drugs for the whole range of severe childhood behavior disorders. This requires intense research and training efforts. Such efforts provide the means for developing, testing and delivering better treatment programs. There is a similar need for research in the techniques of special education and also a need to make these techniques available to children who can benefit. It would appear to be a sound Federal investment to conduct such research and training.

In summary, there is a place for stimulant medications in the treatment of the hyperkinetic behavioral disturbance, but these medications are not the only form of effective treatment. We recommend a code of ethical practices in the promotion of medicines, and candor, meticulous care and restraint on the part of the media, professionals and the public. Expanded programs of continuing education for those concerned with the health care of the young, and also sustained research into their problems, are urgently needed.

Our society is facing a crisis in its competence and willingness to develop and eliver authentic knowledge about complex problems. Without such knowledge, the public annot be protected against half-truths and sensationalism, nor can the public advance its concern for the health of children.

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APPENDICES

I. Referral, medical, demographic, psychiatric, and behavioral measures

II. K-P diet, control diet, and associated dietary measures

III. Diet study flow sheet

IV. Parent and teacher Hyperkinesis Index Scores (raw data)

V. Informal comments of teachers following each diet trial

WESTERN PSYCHIATRIC INSTITUTE AND CLINIC

Name of Patient:____________________ **Age:**__________ D. O. B. :____________

Parents:__________________________ **Telephone:**__________________________

Address:____

Present School:____________________ **Teacher:** ______________ **Grade:**________

Address:__________________________ Principal:__________________________

Source of Referral: Pediatrician's Name and Address:

Nature of Problem:____

Duration of Symptoms:______________________

Previous Treatments:____

Present Medication and Dosage Level:____________________________________

Medical Complications:____

Allergenic Reactions:____

Date of First Appointment:____________________

INFORMED CONSENT

I, the parent (or legal guardian) of ______________________, agree to participate in the study of dietary factors in hyperkinesis. I understand that the purpose of the study is to determine whether either of two special diets is beneficial to my child's behavior, especially in reducing his overactivity and attentional problems. (Message from the Principal Investigator : "In our experience some children improve on one diet and not the other, but a child may show no change to either diet, improve on one and not the other, or improve on both. In this study we hope to find out which children do best on which diet, and whether one diet is better in an overall sense than the other".)

I also understand that the study will last two months, with one month on each diet. I have agreed during this time to adhere as strictly as possible to the prescribed diets, with the understanding that I may consult the study coordinator or the study dietician regarding any problems or questions. It has been explained to me that both diets are nutritionally balanced and pose no medical or nutritional hazards. I may withdraw from the study at any time that I or my family physician deems it advisable for any reason whatsoever. (Message from the Principal Investigator : "If your child has been receiving medication to help his hyperactivity, this medication will have to be stopped during participation in this study. Undoubtedly there is good reason you are treating your child with medication already, so you should be aware of the changes that might occur when medication is stopped. As you know, some children are more impulsive, restless, distractible or troublesome without this form of treatment. You will have to expect that such behaviors may recur when medication is withdrawn. However, you will be free to reinstate the medication whenever these symptoms become too troubling to you or your child, or whenever its absence threatens his school progress or safety in any way, as determined by you, the child, or your physician. We will assist you in every way to manage these symptoms so that you may discover whether one of the diets may obtain comparable or better results".)

No representation has been made to me that these diets will cure the problems of my child, and I fully understand the experimental nature of the program. I have been told that the results of any tests, examinations or treatments will be available to me, and that the progress of the study will involve the cooperation and supervision by a qualified psychiatrist, clinical psychologist, and dietician.

I have been told that ratings of my child's school behavior and performance may be sought as part of the study, and have agreed to give permission to obtain this information for the purposes of the study. All medical, social, and scholastic information or records will be open to me upon request and will be kept strictly confidential. Such records will only be available to the members of the study team or professions or persons for whom I grant specific consent. No publication of any documents or reports will in any way identify my child or his family by name unless this is specifically authorized in writing by me.

I have not been promised any reward, inducement or payment to participate in the study, but have been told that the examinations, tests, and interviews connected with the study are free. Any services required beyond the study itself are my responsibility and I have been told that such services or advice will be given as far as possible within the study, but should further services be required the study team will assist in locating them.

I have been told that this study is supported by the National Institute of Education of the Department of Health, Education, and Welfare, but that the study team assumes full responsibility for the conduct and execution of the study, and the Government of the United States does not assume any responsibility for any medical or legal disputes that may arise out of the study.

Signed______________________________

Witnessed________________________________

Date____________________________________

WESTERN PSYCHIATRIC INSTITUTE AND CLINIC
UNIVERSITY OF PITTSBURGH
3811 O'HARA STREET
PITTSBURGH, PENNSYLVANIA 15261

I, ____________________, mother/father of ________________ give permission to ____________________ to release any relevant information, testing or evaluations regarding my child to WPIC.

Signed: ____________________

Date: ____________________

WESTERN PSYCHIATRIC INSTITUTE AND CLINIC
UNIVERSITY OF PITTSBURGH
3811 O'HARA STREET
PITTSBURGH, PENNSYLVANIA 15261

Dear Doctor:

You may have heard that Ben F. Feingold, M.D., chief emeritus of the allergy department at the Kaiser-Permanente Medical Center in San Francisco, has promulgated the thesis that certain food additives and natural salicylates may cause asthma-like reactions and hyperkinesis in children. Because of the wide publicity given to this claim, the National Institute of Education has solicited a proposal from us to study the effect of food additives on children's behavior. I have recently learned that the contract has been awarded and that we may pursue the study.

Our intent is to do a careful, two month, double-blind trial of Feingold's diet against a control diet utilizing children between the ages of 6 years and 12 years, 11 months who are known to be hyperkinetic. To insure adequate nutrition under each of the two diets, nutritional monitoring and analysis will be performed. All parents will have the opportunity of observing their children under both the experimental and the control diet. However, for the duration of the study, it will be necessary to suspend all prescribed medication for the treatment of hyperactivity.

As a part of the study, the children and their families will receive psychiatric assessment, psychological testing, a neurological examination and follow-up visits. These services are all free of charge. In addition, we will send you information regarding the patient and the progress of the trial.

I have met with the parents of this child, explained the requirements of the study, and they are interested in enrolling their child in this trial. With your approval as the child's pediatrician, we will initiate our initial screnning procedures. If there are any objections on your part to this child serving in this experiment, or for further information, you may call me here at the Western Psychiatric Institute and Clinic, 624-2181.

Thank you for your cooperation.

Yours sincerely,

Charles H. Goyette, Ph.D.
Project Coordinator

WESTERN PSYCHIATRIC INSTITUTE AND CLINIC
UNIVERSITY OF PITTSBURGH
3811 O'HARA STREET
PITTSBURGH, PENNSYLVANIA 15261

Dear

I am writing in reference to _________________________, a student in your _______________ grade class. This child is participating in a study sponsored by the National Institute of Education investigating the effects of diet control on behavior. To obtain an overall measure of this child's response to the treatment program, we would like to obtain information on this student's classroom behavior immediately prior to and during the course of the study. Broken down into actual time on your part, we estimate this will require between 5 and 10 minutes per week recording your behavior observations for a period of approximately 2 months. I should point out that this teacher report is an extremely sensitive measure of symptom change, and your cooperation in observing and recording this child's behavior will provide invaluable information as to the effectiveness of the treatment program under investigation.

I am enclosing a packet of dated teacher questionnaires to assist you in the coding of your observations. Simply complete the rating scale on the date indicated and return it in the pre-addressed envelope provided.

If there are any questions or problems that arise, you may call me here at Western Psychiatric Institute and Clinic, 624-2181.

Thank you again for your cooperation.

Sincerely,

Charles H Goyette

Charles H. Goyette, Ph.D.
Project Coordinator

Enclosures

Child's Name:______________________ Number:_______________

Discharge Summary

Neuropsychiatric:

Family:

History:

Nutritional background:

Follow-up:

COORDINATOR'S DATA CHECKLIST

Patient Name:______________________________ Patient Number:__________________

Current Medication:______________________________________

Office Evaluation:

1. Pure or developmental (normal birth weight; no neonatal trauma, no traumatic CNS insults)
2. Positive neurologic findings
3. Positive or suspect environmental causes (disrupted family, adoption, emotional disturbance)
4. Positive allergy history or condition

Pre-treatment

Parent Questionnaire 000	__________	__________
Abbrev. Parent Q 013	__________	
Abbrev. Parent Q 023	__________	
Abbrev. Parent Q 033	__________	
Abbrev. Parent Q 043	__________	

Baseline

Abbrev. Parent Q 053	__________
Abbrev. Parent Q 063	__________
Abbrev. Parent Q 073	__________
Abbrev. Parent Q 083	__________

Degree of Prior knowledge:______________________________

Diet Assigned: ______________________________

Abbrev. Parent Q 093 __________

Abbrev. Parent Q 103 __________

Abbrev. Parent Q 113 __________

Parent Q 123 __________ __________

Number of infractions reported __________

Dietary Degree of Difficulty __________

Diet Assigned: ______________________________

Abbrev. Parent Q 133 __________

Abbrev. Parent Q 143 __________

Abbrev. Parent Q 153 __________

Parent Q 163 __________ __________

Number of infractions reported __________

Dietary Degree of Difficulty __________

Pre-treatment

Teacher Questionnaire 000 ____________ ____________

Abbrev. Teacher Q 013 ____________

Abbrev. Teacher Q 023 ____________

Abbrev. Teacher Q 033 ____________

Abbrev. Teacher Q 043 ____________

Baseline

Abbrev. Teacher Q 053 ____________

Abbrev. Teacher Q 063 ____________

Abbrev. Teacher Q 073 ____________

Abbrev. Teacher Q 083 ____________

Diet Assigned: ____________________________

Abbrev. Teacher Q 093 ____________

Abbrev. Teacher Q 103 ____________

Abbrev. Teacher Q 113 ____________

Teacher Q 123 ____________ ____________

Diet Assigned: ____________________________

Abbrev. Teacher Q 133 ____________

Abbrev. Teacher Q 143 ____________

Abbrev. Teacher Q 153 ____________

Teacher Q 163 ____________ ____________

Chart # ______________________

Patient's Name ______________________________ Age ______ Sex ☐ MALE ☐ FEMALE
Last First Middle Initial

Doctor's Name ______________________________ Date of first examination ______________________

Source of information provided by:
- ☐ 1. MOTHER
- ☐ 2. FATHER
- ☐ 3. BOTH PARENTS
- ☐ 4. OTHER RELATIVE
- ☐ 5. FOSTER PARENTS
- ☐ 6. SOCIAL AGENCY
- ☐ 7. OTHER - *specify*

Professional identification of observer:
- ☐ 1. NEUROLOGIST
- ☐ 2. PSYCOLOGIST
- ☐ 3. PSYCHIATRIST
- ☐ 4. PEDIATRICIAN
- ☐ 5. SOCIAL WORKER
- ☐ 6. TEACHER
- ☐ 7. PHYSICIAN OTHER - *specify*
- ☐ 8. OTHER - *specify*

Chief complaint *(describe)* ____

____

Reason for referral: ☐ 1. MEDICAL, NEUROLOGICAL ☐ 2. BEHAVIOR ☐ 3. ACADEMIC ☐ 4. OTHER - *specify*
(May check more than one.)

If academic, name three areas of low achievement
1.
2.
3.

Current symptoms referable to system

REMARKS

	NO	YES	UNKNOWN
Neurological	☐	☐	☐
Psychiatric	☐	☐	☐
Cardiovascular	☐	☐	☐
Pulmonary	☐	☐	☐
G.I.	☐	☐	☐
Genitourinary	☐	☐	☐
Endocrine	☐	☐	☐
Blood	☐	☐	☐
Skin	☐	☐	☐
Skeletal	☐	☐	☐
Other, *if yes, specify*	☐	☐	☐

Past illnesses

Head trauma with unconciousness	☐	☐	☐
Skull fracture	☐	☐	☐
Febrile seizures	☐	☐	☐
Hypoglycemic attacks	☐	☐	☐
Meningitis	☐	☐	☐
Encephalitis	☐	☐	☐
Rheumatic fever	☐	☐	☐
Chorea	☐	☐	☐
Measles severe	☐	☐	☐
Rubella severe	☐	☐	☐
Serious infections	☐	☐	☐
CNS reaction to drugs	☐	☐	☐
CNS reaction to vaccines or immunization	☐	☐	☐
Other [illegible] illness in family [illegible]	☐	☐	☐

If yes, specify

[illegible] **REMARKS**

Abortions, previous to this child ☐ NONE ☐ YES ☐ UNKNOWN
If yes, number ____________ or ☐ NUMBER UNKNOWN
Any stillborn or deaths before age 1? ☐ NONE ☐ YES ☐ UNKNOWN
If yes, number ____________ or ☐ NUMBER UNKNOWN

Pregnancy		NO	YES	UNKNOWN	
Blood incompatibility, *if yes, specify*		☐	☐	☐	
Toxemia		☐	☐	☐	
Diabetes		☐	☐	☐	
Rubella		☐	☐	☐	
Other infections		☐	☐	☐	
Major illnesses or trauma	*If yes, specify*	☐	☐	☐	
Drugs		☐	☐	☐	
Pelvic X-Rays		☐	☐	☐	IF YES, NO.
Hemorrhage		☐	☐	☐	
Other abnormalities during pregnancy		☐	☐	☐	

Labor and Delivery	NO	YES	UNKNOWN
Length of gestation - in weeks			☐
Birth weight _____ lbs. _____ oz.			☐
Labor - spontaneous, no complications	☐	☐	☐

If complications, ☐ BREECH ☐ CAESAREAN ☐ OTHER, *specify*

Neonatal distress (up to one month) UNKNOWN
APGAR ☐ 10 ☐ 9 ☐ 8 ☐ 7 ☐ 6 ☐
☐ 5 ☐ 4 ☐ 3 ☐ 2 ☐ 1

	NO	YES	UNKNOWN
Exchange transfusion	☐	☐	☐
Severe jaundice	☐	☐	☐
Anoxia.	☐	☐	☐
Resuscitation	☐	☐	☐
Incubator	☐	☐	☐
Seizures	☐	☐	☐
Poor sucking	☐	☐	☐
Abnormal cry	☐	☐	☐
Others, *specify*	☐	☐	☐

Growth & development including first 2 years of life

	NO	YES	UNKNOWN	
Poor weight gain	☐	☐	☐	
Very infrequent cry	☐	☐	☐	
Abnormal cry	☐	☐	☐	
Colic	☐	☐	☐	
Less than normal sleep	☐	☐	☐	
More than normal sleep	☐	☐	☐	
Over active	☐	☐	☐	
Under active	☐	☐	☐	
Rhythmic abnormal behavior (rocking, head banging)	☐	☐	☐	
Other abnormal behavior	☐	☐	☐	*If yes, specify*

Social & affectional ☐ CLINGING ☐ NORMAL ☐ UNRESPONSIVE

Developmental milestones (first two years)

	UNKNOWN
Sat up unaided at _____ mos.	☐
Walked unassisted at _____ mos.	☐
Using words at _____ mos.	☐

Developmental milestones (after two years)

	UNKNOWN
Speaking in sentences at _____ yrs. _____ mos.	☐
Trained bladder day at _____ yrs. _____ mos.	☐
Trained bowels at _____ yrs. _____ mos.	☐
Bed wetting after age of five ☐ NO ☐ YES	☐
Toilet training ☐ EASY ☐ DIFF.	☐
Tricycle riding at age _____ yrs. _____ mos.	☐
Bicycle riding at age _____ yrs. _____ mos.	☐
Abnormal speech ☐ NO ☐ YES	☐
Handedness ☐ RIGHT ☐ LEFT ☐ AMB.	☐

School History

☐ SCHOOL AGE BUT NO PLACEMENT ATTEMPTED ☐ PRESCHOOL AGE

	EXCELLENT	AVERAGE	POOR	FAILED
Performance in kindergarten	☐	☐	☐	☐
Performance in grade school	☐	☐	☐	☐
Performance in high school	☐	☐	☐	☐

School placement - grade, *specify* _____________	NO	YES	UNKNOWN
Attends regular school or class	☐	☐	☐
Attends regular school, special class (academic)	☐	☐	☐
Attends regular school, special class (behavior)	☐	☐	☐
Out of school	☐	☐	☐
No. of school moves due to behavior _____ moves			☐
No. of school moves due to academic _____ moves			☐

(Omit household moves in both cases)

Family assessment *(mother, father, sibs or other permanent household member only)*

(After box, if yes, specify relationship)	NO	YES	UNKNOWN
Parental deprivation	☐	☐	☐
Cultural deprivation	☐	☐	☐
Neglectful family	☐	☐	☐
Over-protective family	☐	☐	☐
Rejecting family	☐	☐	☐
Excessive punishment	☐	☐	☐
Major psychiatric illness	☐	☐	☐
Sexual deviant behavior	☐	☐	☐
Alcoholism	☐	☐	☐
Criminal record	☐	☐	☐

Parent's education (if living with patient)

	MOTHER	FATHER	UNKNOWN
No education	☐	☐	☐
Grade school - failed	☐	☐	☐
Grade school certificate	☐	☐	☐
High school - failed or quit	☐	☐	☐
High school - diploma	☐	☐	☐
College or equivalent	☐	☐	☐

Race:

MOTHER		FATHER
☐	CAUCASIAN	☐
☐	NEGRO	☐
☐	ORIENTAL	☐
☐	OTHER, *specify*	☐

(Hollingshead 2 factor index of social position)

Group ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5

REMARKS

Mother's age _____ ☐ UNKNOWN DECEASED _____ YRS. AGO
Father's age _____ ☐ UNKNOWN DECEASED _____ YRS. AGO
Ordinal position of child i.e. 3d of 6 = 3 6 ____________

Marital Status - ☐ MARRIED &/OR LIVING TOGETHER ☐ SEPARATED OR DIVORCED
☐ FATHER DEAD ☐ MOTHER DEAD
☐ BOTH PARENTS DEAD

Number of household moves since marriage _____ ☐ NO. UNKNOWN

Childs placement

MOTHER		FATHER
☐	NATURAL PARENT	☐
☐	STEP	☐
☐	ADOPTIVE	☐
☐	PAID FOSTER	☐
☐	INSTITUTION	☐
☐	OTHER - *specify*	☐

Family diseases (mother, father, or sibs only, specify if yes and specify relationship.)

	NO	YES	UNKNOWN
Congenital malformation	☐	☐	☐
Hereditary disease, including neuro disorder	☐	☐	☐
Neuro-psychiatric disorder	☐	☐	☐
Left handedness	☐	☐	☐
Speech difficulty	☐	☐	☐
Reading & writing difficulty	☐	☐	☐
Hyperactivity	☐	☐	☐

ADDITIONAL HISTORY:

Form # 43
6-73

CHILDREN'S PERSONAL DATA INVENTORY

C
P
D
I

INSTRUCTIONS *Insert General Scoring Sheet and Code 10 for Sheet Number. Code 000 for PERIOD.*

Raters are cautioned to be particularly careful in coding their responses since several items have sub-parts which must be coded on the same row. Follow the coding instructions carefully. Complete once for each subject. Please answer all items.

If information is not ascertained, mark a field of "9"s, e.g., 9, 99, 999 etc.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

Mark on right half of scoring sheet on row specified — ROW NO.

IDENTIFICATION (Note: Sex of subject is coded within Patient Number)

a. Subject's Age: Mark time units — 1 = months, 2 = years, on Row 1 and give numeric (2 digits) on Rows 2–3 — 1; 2 3

b. Subject's Race is: *Code both b and c on Row 4* — 4
0 = Caucasoid
1 = Negroid
2 = Mongoloid
3 = Other

c. Has Subject's Residence Been:
5 = Primarily urban
6 = Primarily suburban
7 = Primarily rural

d. Sibling Sequence: Subject is the *enter number (2 digits)* child of *enter number (2 digits)* children. (Only child is coded "the 01 child of 01 children".) — 5 6; 7 8

e. Is Subject One of Twins, Triplets, etc.? — 9
0 = No
1 = Yes, homozygous
2 = Yes, heterozygous
3 = Yes, unknown zygosity

f. The Subject's Present Family Constellation Consists of: *(Mark all applicable on Row 10)* — 10
0 = Natural mother
1 = Natural father
2 = Step-parent
3 = Adoptive parents
4 = Foster parents
5 = Adult relatives (grandparents, uncles, aunts, etc.)
6 = Siblings, step-siblings and/or other children
7 = Subject not living with family, is in non-psychiatric institution
8 = Subject not living with family, is in psychiatric institution/hospital

PARENTS' DEMOGRAPHY

Is either NATURAL parent: *Code both a and b on Row 11* — 11

a. Dead?
0 = No
1 = Yes, mother
2 = Yes, father
3 = Yes, both

b. Divorced or out of home?
5 = No
6 = Yes, mother
7 = Yes, father
8 = Yes, both

Mother's Age: Mother or mother surrogate presently in the home *(2 digits)* (99 = Not applicable) — 12 13

Father's Age: Father or father surrogate presently in the home *(2 digits)* (99 = Not applicable) — 14 15

Row										
1	0	1	2	3	4	5	6	7	8	9
2	0	1	2	3	4	5	6	7	8	9
3	0	1	2	3	4	5	6	7	8	9
4	0	1	2	3	4	5	6	7	8	9
5	0	1	2	3	4	5	6	7	8	9
6	0	1	2	3	4	5	6	7	8	9
7	0	1	2	3	4	5	6	7	8	9
8	0	1	2	3	4	5	6	7	8	9
9	0	1	2	3	4	5	6	7	8	9
10	0	1	2	3	4	5	6	7	8	9
11	0	1	2	3	4	5	6	7	8	9
12	0	1	2	3	4	5	6	7	8	9
13	0	1	2	3	4	5	6	7	8	9
14	0	1	2	3	4	5	6	7	8	9
15	0	1	2	3	4	5	6	7	8	9
16	0	1	2	3	4	5	6	7	8	9
17	0	1	2	3	4	5	6	7	8	9
18	0	1	2	3	4	5	6	7	8	9
19	0	1	2	3	4	5	6	7	8	9
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29	0	1	2	3	4	5	6	7	8	9
30	0	1	2	3	4	5	6	7	8	9
31	0	1	2	3	4	5	6	7	8	9
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33	0	1	2	3	4	5	6	7	8	9
34	0	1	2	3	4	5	6	7	8	9
35	0	1	2	3	4	5	6	7	8	9
36	0	1	2	3	4	5	6	7	8	9
37	0	1	2	3	4	5	6	7	8	9
38	0	1	2	3	4	5	6	7	8	9
39	0	1	2	3	4	5	6	7	8	9
40	0	1	2	3	4	5	6	7	8	9

INSTRUCTIONS *Insert General Scoring Sheet and Code 10 for Sheet Number. Code 000 for PERIOD.*

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If information is not ascertained, mark a field of "9"s, e.g., 9, 99, 999 etc.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

Continue marking on right half of scoring sheet on row specified — ROW NO.

PARENTS' EDUCATION

e. Mother or Present Surrogate *Code highest level attained for MOTHER* 16

f. Father or Present Surrogate *Code highest level attained for FATHER* 17

0 = Not applicable
1 = Graduate professional training
2 = College graduate
3 = Some college or technical school
4 = High school graduate
5 = Some high school (10-11)
6 = Junior high school (7, 8, 9)
7 = Less than 7 years of school
9 = Not ascertained

PARENTS' OCCUPATION

g. Mother's or Female Surrogate's Present Occupational Status is: 18

h. Father or Male Surrogate's Present Occupational Status is: 19

Use this code for g and h:
0 = Not applicable
1 = Full time gainful employment
2 = Part time gainful employment
3 = Unemployed
4 = Dependent spouse or student
5 = Recipient of public or private assistance

i. Mother's or Female Surrogate's Highest Occupational Attainment is: . . 20

j. Fathers or Male Surrogate's Highest Occupational Attainment is: . . . 21

Use this code for i and j. *See Manual for detailed list of occupations.*
1 = Higher executive, proprietor of large concern, major professional
2 = Business manager of large concern, proprietor of medium sized business, lesser professional
3 = Administrative personnel, owner of small independent business, minor professional
4 = Clerical or sales worker, technician, owner of little business
5 = Skilled manual employee
6 = Machine operator, semi-skilled employee
7 = Unskilled employee
8 = Never worked in paid employment
9 = Not ascertained

Has either parent or present surrogate been:
Mark one response for each item using this code: 0 = Neither parent 1 = Mother 2 = Father 3 = Both parents

k. Out of home (3 months or longer) due to physical or mental illness . . . 22
Separated (3 months or longer) due to marital difficulties 23
Cruel or abusive (to patient, spouse, siblings, etc.) 24
Not a steady worker or competent housewife 25

CPDI L-2

Row									
1	0	1	2	3	4	5	6	7	8
2	0	1	2	3	4	5	6	7	8
3	0	1	2	3	4	5	6	7	8
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37	0	1	2	3	4	5	6	7	8
38	0	1	2	3	4	5	6	7	8
39	0	1	2	3	4	5	6	7	8
40	0	1	2	3	4	5	6	7	8
41	0	1	2	3	4	5	6	7	8
Col	11	12	13	14	15	16	17	18	19

INSTRUCTIONS *Insert General Scoring Sheet and Code 10 for Sheet Number. Code 000 for PERIOD.*

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If information is not ascertained, mark a field of "9"s, e.g., 9, 99, 999 etc.

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Continue marking on right half of scoring sheet on row specified — ROW NO.

FAMILY HISTORY OF PSYCHIATRIC ILLNESS

Has there been a history of psychiatric illness in family member/s?

Mark all applicable for each item using this code:

0 = None of the members
1 = Natural mother
2 = Natural father
3 = Siblings
5 = Present mother surrogate
6 = Present father surrogate

Non-psychotic psychiatric disturbance	26
Manic depressive disturbance	27
Other major affective disturbance	28
Schizophrenia	29
Other psychotic disturbance	30
Hospitalized for any psychiatric illness	31
Mental deficiency	32
Excessive use of alcohol	33
Excessive use of drugs	34
Imprisonment	35

SUBJECT'S HISTORY OF PSYCHIATRIC ILLNESS

Treatment Status — *Code both a and b on Row 36* — 36

a. Subject is presently: *(Mark one)*
1 = Not in any type of psychiatric treatment
2 = In psychiatric treatment as an outpatient
3 = In partial hospitalization, e.g., day or night hospital, halfway house, etc.
4 = Hospitalized (24 hour)

Prior to this episode, subject has: *(Mark all applicable)*
5 = Never had any type of psychiatric treatment
6 = Received psychiatric outpatient treatment
7 = Received treatment in partial hospitalization setting
8 = Received treatment in 24 hour hospital

"Psychiatric treatment" should be interpreted broadly to include all forms of therapy whose basic function is the alleviation of emotional, behavioral or mental disturbance. "Partial hospitalization" and 24 hour hospitalization include all forms of treatment environments in which the subject spends a substantial part of the day or, in the latter case, the full day.

Age *(years)* when first received treatment for psychiatric illness *(2 digits)* — 37-38
(00) = Never treated

Estimate total duration of ALL outpatient psychiatric treatment — exclusive of present episode — 39-41

Give time units *(0 = days, 1 = weeks, 2 = months, 3 = years)* and duration *(2 digits)*

EXAMPLE: Subject's total treatment amounts to 10 months
Code: 210   000 = No treatment or unknown

n all pages on this side and continue with item 4 on II - 1   L-3

Row 1	0	1	2	3	4	5	6	7	8
2	0	1	2	3	4	5	6	7	8
3	0	1	2	3	4	5	6	7	8
4	0	1	2	3	4	5	6	7	8
5	0	1	2	3	4	5	6	7	8
6	0	1	2	3	4	5	6	7	8
7	0	1	2	3	4	5	6	7	8
8	0	1	2	3	4	5	6	7	8
9	0	1	2	3	4	5	6	7	8
10	0	1	2	3	4	5	6	7	8
11	0	1	2	3	4	5	6	7	8
12	0	1	2	3	4	5	6	7	8
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24	0	1	2	3	4	5	6	7	8
25	0	1	2	3	4	5	6	7	8
26	0	1	2	3	4	5	6	7	8
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28	0	1	2	3	4	5	6	7	8
29	0	1	2	3	4	5	6	7	8
30	0	1	2	3	4	5	6	7	8
31	0	1	2	3	4	5	6	7	8
32	0	1	2	3	4	5	6	7	8
33	0	1	2	3	4	5	6	7	8
34	0	1	2	3	4	5	6	7	8
35	0	1	2	3	4	5	6	7	8
36	0	1	2	3	4	5	6	7	8
37	0	1	2	3	4	5	6	7	8
38	0	1	2	3	4	5	6	7	8
39	0	1	2	3	4	5	6	7	8
40	0	1	2	3	4	5	6	7	8
41	0	1	2	3	4	5	6	7	8
Cols	11	12	13	14	15	16	17	18	19

INSTRUCTIONS *Insert General Scoring Sheet and Code 10 for Sheet Number. Code 000 for PERIOD*

Raters are cautioned to be particularly careful in coding their responses since several items **have** sub parts which must be coded on the same row. Follow the coding instructions carefully. **Complete** once for each subject. Please answer all items.

If information is not ascertained, mark a field of "9"s, e.g., 9, 99, 999 etc.

C
S
H

NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

1	0	1	2	3	4	5	6	7	8	9
2	0	1	2	3	4	5	6	7	8	9
3	0	1	2	3	4	5	6	7	8	9
4	0	1	2	3	4	5	6	7	8	9
5	0	1	2	3	4	5	6	7	8	9
6	0	1	2	3	4	5	6	7	8	9
7	0	1	2	3	4	5	6	7	8	9
8	0	1	2	3	4	5	6	7	8	9
9	0	1	2	3	4	5	6	7	8	9
10	0	1	2	3	4	5	6	7	8	9
11	0	1	2	3	4	5	6	7	8	9
12	0	1	2	3	4	5	6	7	8	9
13	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9
	0	1	2	3	4	5	6	7	8	9

ROW NO.		*Mark on left half of scoring sheet on row specified*
	4.	*SUBJECT'S HISTORY OF PSYCHIATRIC ILLNESS – Continued*
1-3	e.	Estimate total duration of ALL partial hospitalization – exclusive of present episode Give time units *(0 = days; 1 = weeks; 2 = months; 3 = years)* and duration *(2 digits)* 000 = No partial hospitalization
4-6	f.	Estimate total duration of ALL hospitalizations *(24 hour)* exclusive of present episode Give time units *(0 = days; 1 = weeks; 2 = months; 3 = years)* and duration *(2 digits)* EXAMPLE: Subject's total hospitalization amounts to 4 years Code 304 000 = No hospitalizations
7-9	g.	Duration of present episode Mark whether coded in 0 = days 1 = weeks 2 = months 3 = years and give duration *(2 digits)* 000 = Not applicable
	5.	SUBJECT'S DEVELOPMENTAL HISTORY *Code a, b and c on Row 10*
10	a.	Pregnancy and Neonatal Course Were: 0 = Normal 1 = Suspected abnormalities 2 = Definite abnormalities 3 = Not ascertained
	b.	Were there infant feeding problems? 4 = YES 5 = NO 6 = Not ascertained
	c.	Colic? 7 = YES 8 = NO 9 = Not ascertained
		For each of the following items d through h, record months in 2 digits and judge rate of development on next row
11-12 13	d.	Age *(months)* first ate solids - not pureed or strained food Considered 0 = Slow 1 = Normal 2 = Fast
14-15 16	e.	Age *(months)* first fed self with a spoon Considered 0 = Slow 1 = Normal 2 = Fast
17-18 19	f.	Age *(months)* sat unsupported Considered 0 = Slow 1 = Normal 2 = Fast
20-21 22	g.	Age *(months)* first walked by self without holding on Considered 0 = Slow 1 = Normal 2 = Fast
23-24 25	h.	Age *(months)* first words other than Mama and Dadda Considered 0 = Slow 1 = Normal 2 = Fast

R-1 CPOI *Turn page to continue item 5*

INSTRUCTIONS: *Insert General Scoring Sheet and Code 10 for Sheet Number. Code 0x0 for PERIOD.*

Raters are cautioned to be particularly careful in coding their responses since several items **have** sub parts which must be coded on the same row. Follow the coding instructions carefully. **Complete** once for each subject. Please answer all items.

If information is not ascertained, mark a field of "9"s, e.g., 9, 99, 999 etc.

A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

1	0	1	2	3	4	5	6	7	8	9
2	0	1	2	3	4	5	6	7	8	9
3	0	1	2	3	4	5	6	7	8	9
4	0	1	2	3	4	5	6	7	8	9
5	0	1	2	3	4	5	6	7	8	9
6	0	1	2	3	4	5	6	7	8	9
7	0	1	2	3	4	5	6	7	8	9
8	0	1	2	3	4	5	6	7	8	9
9	0	1	2	3	4	5	6	7	8	9
10	0	1	2	3	4	5	6	7	8	9
11	0	1	2	3	4	5	6	7	8	9
12	0	1	2	3	4	5	6	7	8	9
13	0	1	2	3	4	5	6	7	8	9
14	0	1	2	3	4	5	6	7	8	9
15	0	1	2	3	4	5	6	7	8	9
16	0	1	2	3	4	5	6	7	8	9
17	0	1	2	3	4	5	6	7	8	9
18	0	1	2	3	4	5	6	7	8	9
19	0	1	2	3	4	5	6	7	8	9
20	0	1	2	3	4	5	6	7	8	9
21	0	1	2	3	4	5	6	7	8	9
22	0	1	2	3	4	5	6	7	8	9
23	0	1	2	3	4	5	6	7	8	9
24	0	1	2	3	4	5	6	7	8	9
25	0	1	2	3	4	5	6	7	8	9
26	0	1	2	3	4	5	6	7	8	9
27	0	1	2	3	4	5	6	7	8	9
28	0	1	2	3	4	5	6	7	8	9
29	0	1	2	3	4	5	6	7	8	9
30	0	1	2	3	4	5	6	7	8	9
31	0	1	2	3	4	5	6	7	8	9
32	0	1	2	3	4	5	6	7	8	9
33	0	1	2	3	4	5	6	7	8	9
34	0	1	2	3	4	5	6	7	8	9
35	0	1	2	3	4	5	6	7	8	9
36	0	1	2	3	4	5	6	7	8	9
37	0	1	2	3	4	5	6	7	8	9
38	0	1	2	3	4	5	6	7	8	9
39	0	1	2	3	4	5	6	7	8	9
40	0	1	2	3	4	5	6	7	8	9
	1	2	3	4	5	6	7	8	9	10

ROW NO.		*Continue marking on left half of scoring sheet on row spec*
26 27 28	i.	**Age** *(months)* of speaking 3 word sentences Considered: 0 = Slow, 1 = Normal, 2 = Fast
29 30 31	j.	**Age** *(months)* trained bladder during day Considered: 0 = Slow, 1 = Normal, 2 = Fast
32 33 34	k.	**Age** *(months)* trained bowels Considered: 0 = Slow, 1 = Normal, 2 = Fast
35 36	l.	**Age** *(years)* began menstruating *(2 digits)* 00 = Not applicable
37		*Mark m, n and o all on Row 37*
	m.	Masturbates? 0 = NO 1 = YES 2 = Not ascertained
	n.	Does he/she dress in clothes or play with toys of opposite sex? 3 = NO 4 = YES 5 = Not ascertained
	o.	Does he/she express a desire to grow up to be a member of opposite sex? 6 = NO 7 = YES 9 = Not ascertained
	6.	SUBJECT'S SCHOOL HISTORY
38 39	a.	Current Grade Placement *(2 digits)* *Number grades 01 – 12* 20 = Preschool 23 = Special or Ungraded 21 = Nursery 24 = Not in school 22 = Kindergarten
40		*Mark both b and c on Row 20*
	b.	Child's School History is **Best Characterized by:** 0 = Not applicable 1 = No significant problems at any time 2 = Minor problems or occasional difficulties 3 = Major problems seen only in current year 4 = Major problems through school history with [illegible] of [illegible] 5 = Major problems almost continually since entrance into school
	c.	In General Academic Achievement Has Been: 6 = Above average 7 = Average 8 = Below average
	7.	ATTITUDE TOWARD PRESENT TREATMENT
41		At pretreatment, the attitudes of the child and his parents were: *Make 2 marks (one for child, one for family) on Row 41* 0 Child positive 5 Family positive 1 Child ambivalent 6 Family ambivalent 2 [illegible] 7 [illegible] 3 [illegible] 8 [illegible] 4 Child's attitude not ascertained 9 Family attitude not ascertained

R-2 CPDI END

Dear

Thank you for participating in this study. Your recording of observations is most helpful to us. We would like to remind you to continue with the dated questionnaires as their completion is imperative to the success of the study. If there are any problems or questions, please feel free to contact Ms. Southwick at 624-2035. Thank you again.

Sincerely,

CHARLES GOYETTE, Ph.D.

APPENDIX III*

Teacher Questionnaire

The Teacher Questionnaire (TQ) is a 39-item symptom list to be filled out by the child's home-room teacher. Two forms for initial and followup ratings are identical except for background information included on the preliminary school report. The items are divided into three large groupings: classroom behavior, group participation, and attitude toward authority. Ten items (5, 6, 14, 8, 1, 7, 3, 13, 16, and 21) are also included in the Parent Symptom Questionnaire (PSQ) and may be used as a separate, brief scale (abbreviated symptom scale) for more frequent assessments of behavior during the course of study.

The factor analysis of the TQ (Conners, 1969) was based on a slightly reworded version of the scale. Factor scores may be obtained from the present version by summing item weights (0, 1, 2, 3) according to the table below.

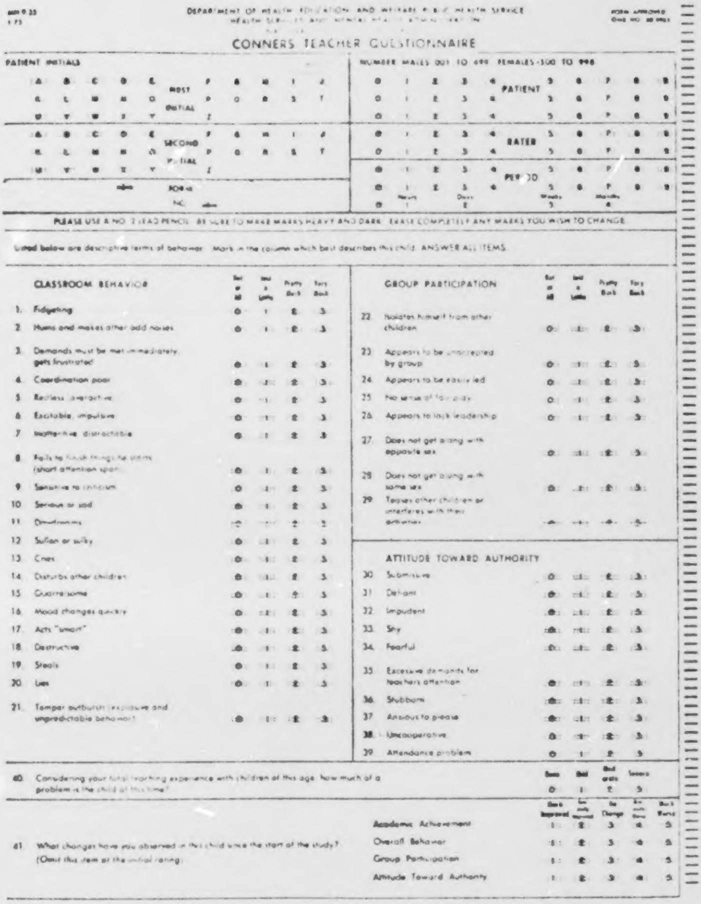
Factor scores will have some degree of intercorrelation, especially between Factors I and IV. (These two Factors might be summed together for some analyses to attain greater reliability of scores.)

Factor Title	Items to be Summed	No. of Items
I. Conduct Problem	12, 15, 17, 18, 19, 20, 21, -30**, 25, 31, 32, 36, 38	13
II. Inattentive-Passive	4, 7, 8, 11, 24, 26	6
III. Tension-Anxiety	9, 10, 30, 33, 34, -39**	6
IV. Hyperactivity	1, 2, 5, 6, 14, 29	6
		31

*Reference No. 11, page 29

**Note that these scores are subtracted from the sum

Reference No. 11, page 29
Conners, C. K. A teacher rating scale for use
in drug studies with children. Amer. J.
Psychiat., 126:884-888, 1969.



[illegible]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE PUBLIC HEALTH SERVICE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION

FORM APPROVED
[illegible]

CONNERS TEACHER QUESTIONNAIRE

PATIENT INITIALS

A	B	C	D	E	FIRST INITIAL	F	G	H	I	J
K	L	M	N	O		P	Q	R	S	T
U	V	W	X	Y		Z				
A	B	C	D	E	SECOND INITIAL	F	G	H	I	J
K	L	M	N	O		P	Q	R	S	T
U	V	W	X	Y		Z				

NUMBER MALES 001 TO 499 FEMALES 500 TO 998

0	1	2	3	4	PATIENT	5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	1	2	3	4	RATER	5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	1	2	3	4	PERIOD	5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	Hours 1		Days 2			Weeks 3		Months 4		

FORM NO.

PLEASE USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

Listed below are descriptive terms of behavior. Mark in the column which best describes this child. ANSWER ALL ITEMS.

CLASSROOM BEHAVIOR	Not at All	Just a Little	Pretty Much	Very Much
1. Fidgeting	0	1	2	3
2. Hums and makes other odd noises	0	1	2	3
3. Demands must be met immediately, gets frustrated	0	1	2	3
4. Coordination poor	0	1	2	3
5. Restless or overactive	0	1	2	3
6. Excitable, impulsive	0	1	2	3
7. Inattentive, distractable	0	1	2	3
8. Fails to finish things he starts (short attention span)	0	1	2	3
9. Sensitive to criticism	0	1	2	3
10. Serious or sad	0	1	2	3
11. Daydreams	0	1	2	3
12. Sullen or sulky	0	1	2	3
13. Cries	0	1	2	3
14. Disturbs other children	0	1	2	3
15. Quarrelsome	0	1	2	3
16. Mood changes quickly	0	1	2	3
17. Acts "smart"	0	1	2	3
18. Destructive	0	1	2	3
19. Steals	0	1	2	3
20. Lies	0	1	2	3
21. Temper outbursts (explosive and unpredictable behavior)	0	1	2	3

GROUP PARTICIPATION	Not at All	Just a Little	Pretty Much	Very Much
22. Isolates himself from other children	0	1	2	3
23. Appears to be unaccepted by group	0	1	2	3
24. Appears to be easily led	0	1	2	3
25. No sense of fair play	0	1	2	3
26. Appears to lack leadership	0	1	2	3
27. Does not get along with opposite sex	0	1	2	3
28. Does not get along with same sex	0	1	2	3
29. Teases other children or interferes with their activities	0	1	2	3

ATTITUDE TOWARD AUTHORITY				
30. Submissive	0	1	2	3
31. Defiant	0	1	2	3
32. Impudent	0	1	2	3
33. Shy	0	1	2	3
34. Fearful	0	1	2	3
35. Excessive demands for teachers attention	0	1	2	3
36. Stubborn	0	1	2	3
37. Anxious to please	0	1	2	3
38. Uncooperative	0	1	2	3
39. Attendance problem	0	1	2	3

	None	Mild	Moderate	Severe
40. Considering your total teaching experience with children of this age, how much of a problem is the child at this time?	0	1	2	3

41. What changes have you observed in this child since the start of the study? (Omit this item at the initial rating)

	Much Improved	Somewhat Improved	No Change	Somewhat Worse	Much Worse
Academic Achievement	1	2	3	4	5
Overall Behavior	1	2	3	4	5
Group Participation	1	2	3	4	5
Attitude Toward Authority	1	2	3	4	5

[illegible]

MH 9-37
[illegible]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

Form Approved
OMB No. [illegible]

CONNERS PARENT-TEACHER QUESTIONNAIRE

PATIENT INITIALS

A	B	C	D	E	FIRST INITIAL	F	G	H	I	J
K	L	M	N	O		P	Q	R	S	T
U	V	W	X	Y		Z				
A	B	C	D	E	SECOND INITIAL	F	G	H	I	J
K	L	M	N	O		P	Q	R	S	T
U	V	W	X	Y		Z				

FORM NO.

NUMBER MALES 001 TO 499 FEMALES 500 TO 998

0	1	2	3	4	PATIENT	5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	1	2	3	4	RATER	5	6	7	8	9
0	1 M 1	2 F 2	3	4		5	6	7	8	9
0	1	2	3	4	PERIOD	5	6	7	8	9
0	1	2	3	4		5	6	7	8	9
0	Hours 1		Days 2			Weeks 3		Months 4		

PLEASE USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

INSTRUCTIONS: Listed below are items concerning children's behavior or the problems they sometimes have. **Read each** item carefully and decide how much you think this child has been bothered by **this problem** at this time: NOT AT ALL, JUST A LITTLE, PRETTY MUCH, or VERY MUCH. **Indicate** your choice by filling **in** the space (▬) in the appropriate column to the right **of each item**.

ANSWER ALL ITEMS

	Not at All	Just a Little	Pretty Much	Very Much
1. **Restless** (overactive)	0	1	2	3
2. **Excitable**, impulsive	0	1	2	3
3. Disturbs other children	0	1	2	3
4. **Fails to finish** things he starts (short attention span)	0	1	2	3
5. Fidgeting	0	1	2	3
6. **Inattentive**, distractable	0	1	2	3
7. **Demands** must be met immediately; frustrated	0	1	2	3
8. Cries	0	1	2	3
9. **Mood** changes quickly	0	1	2	3
10. **Temper** outbursts (explosive and unpredictable behavior)	0	1	2	3

	None	Minor	Moderate	Severe
How **serious** a problem do you think this child has at this time?	0	1	2	3

[illegible]

APPENDIX VI*

Parent Symptom Questionnaire*

The Parent Symptom Questionnaire (PSQ) is a item check list of symptoms most commonly associated with behavior disorders of childhood. The symptoms are rated on a 4-point scale by either one or both parents of a child. Instructions are simply to rate the presence and severity of symptoms in the child as *he is currently functioning* (not as he functioned earlier, i.e., more than one month prior to the evaluation).

Scoring is achieved in the following manner. The item weights (0, 1, 2, 3) are summed to give a total symptom score. This should be prorated for items not answered or mentioned by the parent as not applicable.

The list has been factor analyzed on a sample of clinic outpatients and normal children (N = 683) and has been shown to give relatively stable factor structure across ages and a wide social class range (Conners, 1970). The list has been slightly revised and reworded to include 10 items in common with the *School Symptom Questionnaire* (SSQ). These 10 items are among those most frequently checked by parents and teachers of outpatient children and have been found to be relatively sensitive to drug changes. The brief 10 item scale [Abbreviated Symptom Questionnaire (ASQ)] is useful when frequent reports from parents or teachers need to be assessed during the course of study. The ASQ consists of items 52, 53, 49, 54, 80, 79, 85, 88, 91, and 55 from the PSQ.

Factor scores are obtained by summing the weights for 42 of the PSQ items according to the Table below.

These factor scores will be relatively independent since items were selected so as to have minimal overlap in loadings on other factors. (But some correlation among scales can be expected since only factor scores derived by using actual loadings will be orthogonal to other factors.)

Parents are also asked to indicate those "target symptoms" of most concern. Those items should be scored separately for analyses of drug effects if maximal sensitivity to change is to be obtained.

---

*See Parent's Questionnaire, page 56.

Table

	Factor Title	Items to be Summed	No. of Items
I.	Conduct Problem	39, 40, 41, 47, 48, 51, 69	7
II.	Anxiety	8, 9, 10, 11, 42, 64, 43	7
III.	Impulsive-Hyperactive	79, 80, 81, 82, 83, 84, 89, 90	8
IV.	Learning Problem	45, 62, 63, 67	4
V.	Psychosomatic	6, 21, 22, 23, 24	5
VI	Perfectionism	76, 77, 78	3
VII.	Antisocial	71, 72, 73, 75	4
VIII.	Muscular Tension	12, 13, 14, 36	4
			42

38 items with loadings > .40
4 items with loadings > .35

Reference

Conners, C. K. Symptom patterns in hyperkinetic, neurotic, and normal children. *Child Development*, 41:667-682, 1970.

[illegible]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

Form Approved
OMB No. [illegible]

CONNERS PARENT QUESTIONNAIRE

ALES 500 TO 999					
ENT	5	6	7	8	9
	5	6	7	8	9
	5	6	7	8	9
TER	5	6	7	8	9
	5	6	7	8	9
100	5	6	7	8	9
	5	6	7	8	9
	Weeks 3		Months 4 r		

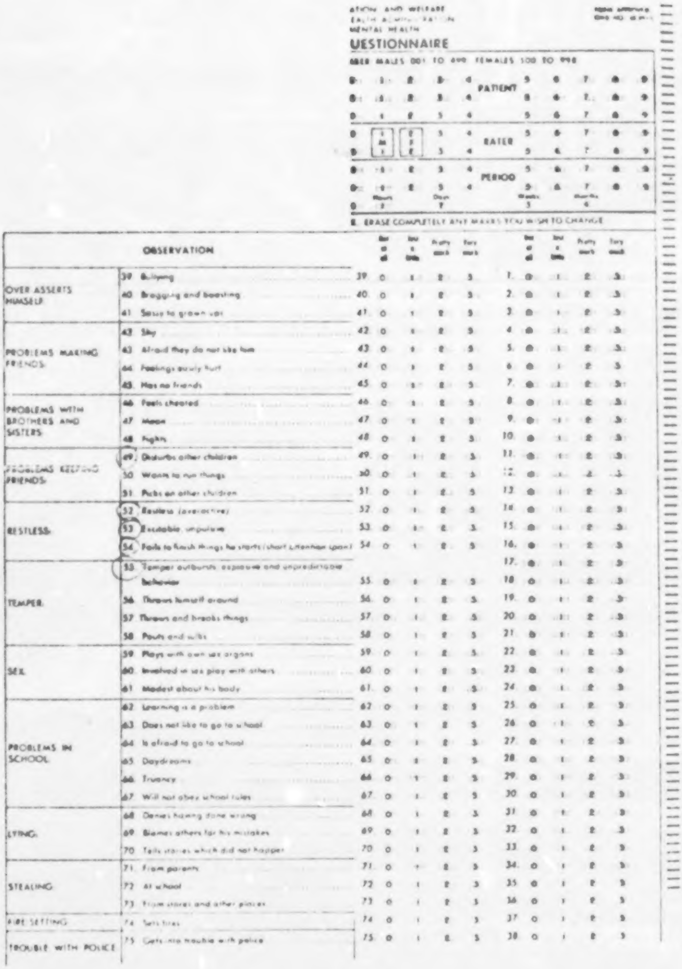
S YOU WISH TO CHANGE

INSTRUCTIONS Listed below are items concerning children's behavior or the problems they sometimes have. Read each item carefully and decide how much you think your child has been bothered by this problem during the last month: NOT AT ALL, JUST A LITTLE, PRETTY MUCH, or VERY MUCH.

Indicate your choice by filling in the space (▬) in the appropriate column to the right of each item.

ANSWER ALL ITEMS

OBSERVATION			Not at all	Just a little	Pretty much	Very much
PROBLEMS OF EATING	1. Picky and finicky	1.	0	1	2	3
	2. Will not eat enough	2.	0	1	2	3
	3. Overweight	3.	0	1	2	3
PROBLEMS OF SLEEP	4. Restless	4.	0	1	2	3
	5. Nightmares	5.	0	1	2	3
	6. Awakens at night	6.	0	1	2	3
	7. Cannot fall asleep	7.	0	1	2	3
FEAR AND WORRIES	8. Afraid of new situations	8.	0	1	2	3
	9. Afraid of people	9.	0	1	2	3
	10. Afraid of being alone	10.	0	1	2	3
	11. Worries about illness and death	11.	0	1	2	3
MUSCULAR TENSION	12. Gets stiff and rigid	12.	0	1	2	3
	13. Twitches, jerks, etc.	13.	0	1	2	3
	14. Shakes	14.	0	1	2	3
SPEECH PROBLEMS	15. Stuttering	15.	0	1	2	3
	16. Hard to understand	16.	0	1	2	3
WETTING	17. Bed wetting	17.	0	1	2	3
	18. Runs to bathroom	18.	0	1	2	3
BOWEL PROBLEMS	19. Soiling self	19.	0	1	2	3
	20. Holds back bowel movements	20.	0	1	2	3
COMPLAINS OF FOLLOWING SYMPTOMS EVEN THOUGH DOCTOR CAN FIND NOTHING WRONG	21. Headaches	21.	0	1	2	3
	22. Stomachaches	22.	0	1	2	3
	23. Vomiting	23.	0	1	2	3
	24. Aches and pains	24.	0	1	2	3
	25. Loose bowels	25.	0	1	2	3
PROBLEMS OF SUCKING, CHEWING, or PICKING	26. Sucks thumb	26.	0	1	2	3
	27. Bites or picks nails	27.	0	1	2	3
	28. Chews on clothes, blankets, or others	28.	0	1	2	3
	29. Picks at things such as hair, clothing, etc.	29.	0	1	2	3
CHILDISH OR IMMATURE	30. Does not act his age	30.	0	1	2	3
	31. Cries	31.	0	1	2	3
	32. Wants help doing things he should do alone	32.	0	1	2	3
	33. Clings to parents or other adults	33.	0	1	2	3
	34. Baby talk	34.	0	1	2	3
TROUBLE WITH FEELINGS	35. Keeps anger to himself	35.	0	1	2	3
	36. Lets himself get pushed around by other children	36.	0	1	2	3
	37. Unhappy	37.	0	1	2	3
	38. Carries a chip on his shoulder	38.	0	1	2	3



ATION AND WELFARE
EALTH ADMINISTRATION
MENTAL HEALTH

[illegible]

UESTIONNAIRE

BER MALES 001 TO 499 FEMALES 500 TO 998

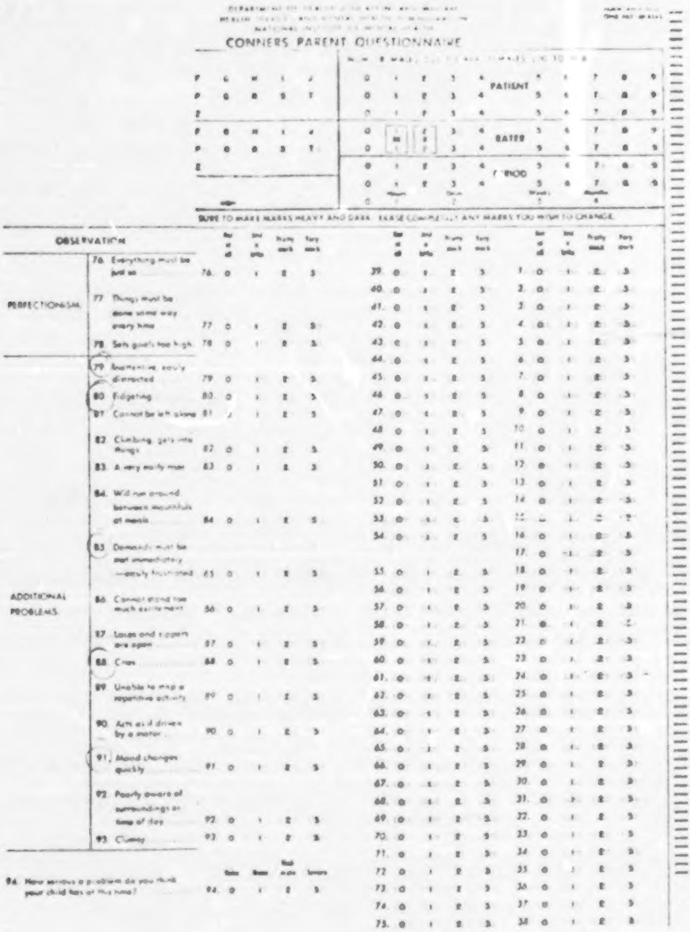
PATIENT
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9

RATER
0 1 M 1 2 F 2 3 4 5 6 7 8 9
0 3 4 5 6 7 8 9

PERIOD
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 Hours 1 Days 2 Weeks 3 Months 4

ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE

OBSERVATION			Not at all	Just a little	Pretty much	Very much		Not at all	Just a little	Pretty much	Very much
OVER ASSERTS HIMSELF	39 Bullying	39.	0	1	2	3	1.	0	1	2	3
	40 Bragging and boasting	40.	0	1	2	3	2.	0	1	2	3
	41 Sassy to grown ups	41.	0	1	2	3	3.	0	1	2	3
PROBLEMS MAKING FRIENDS	42 Shy	42.	0	1	2	3	4.	0	1	2	3
	43 Afraid they do not like him	43.	0	1	2	3	5.	0	1	2	3
	44 Feelings easily hurt	44.	0	1	2	3	6.	0	1	2	3
	45. Has no friends	45.	0	1	2	3	7.	0	1	2	3
PROBLEMS WITH BROTHERS AND SISTERS	46 Feels cheated	46.	0	1	2	3	8.	0	1	2	3
	47 Mean	47.	0	1	2	3	9.	0	1	2	3
	48 Fights	48.	0	1	2	3	10.	0	1	2	3
PROBLEMS KEEPING FRIENDS	49. Disturbs other children	49.	0	1	2	3	11.	0	1	2	3
	50 Wants to run things	50.	0	1	2	3	12.	0	1	2	3
	51 Picks on other children	51.	0	1	2	3	13.	0	1	2	3
RESTLESS	52 Restless (overactive)	52.	0	1	2	3	14.	0	1	2	3
	53 Excitable, impulsive	53.	0	1	2	3	15.	0	1	2	3
	54 Fails to finish things he starts (short attention span)	54.	0	1	2	3	16.	0	1	2	3
							17.	0	1	2	3
TEMPER	55 Temper outbursts, explosive and unpredictable behavior	55.	0	1	2	3	18.	0	1	2	3
	56 Throws himself around	56.	0	1	2	3	19.	0	1	2	3
	57 Throws and breaks things	57.	0	1	2	3	20.	0	1	2	3
	58 Pouts and sulks	58.	0	1	2	3	21.	0	1	2	3
SEX	59 Plays with own sex organs	59.	0	1	2	3	22.	0	1	2	3
	60. Involved in sex play with others	60.	0	1	2	3	23.	0	1	2	3
	61 Modest about his body	61.	0	1	2	3	24.	0	1	2	3
PROBLEMS IN SCHOOL	62 Learning is a problem	62.	0	1	2	3	25.	0	1	2	3
	63 Does not like to go to school	63.	0	1	2	3	26.	0	1	2	3
	64 Is afraid to go to school	64.	0	1	2	3	27.	0	1	2	3
	65 Daydreams	65.	0	1	2	3	28.	0	1	2	3
	66 Truancy	66.	0	1	2	3	29.	0	1	2	3
	67 Will not obey school rules	67.	0	1	2	3	30.	0	1	2	3
LYING	68 Denies having done wrong	68.	0	1	2	3	31.	0	1	2	3
	69 Blames others for his mistakes	69.	0	1	2	3	32.	0	1	2	3
	70 Tells stories which did not happen	70.	0	1	2	3	33.	0	1	2	3
STEALING	71 From parents	71.	0	1	2	3	34.	0	1	2	3
	72 At school	72.	0	1	2	3	35.	0	1	2	3
	73 From stores and other places	73.	0	1	2	3	36.	0	1	2	3
FIRE SETTING	74 Sets fires	74.	0	1	2	3	37.	0	1	2	3
TROUBLE WITH POLICE	75 Gets into trouble with police	75.	0	1	2	3	38.	0	1	2	3



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

CONNERS PARENT QUESTIONNAIRE

PATIENT

RATER

PERIOD

Hours 1 Days 2 Weeks 3 Months 4

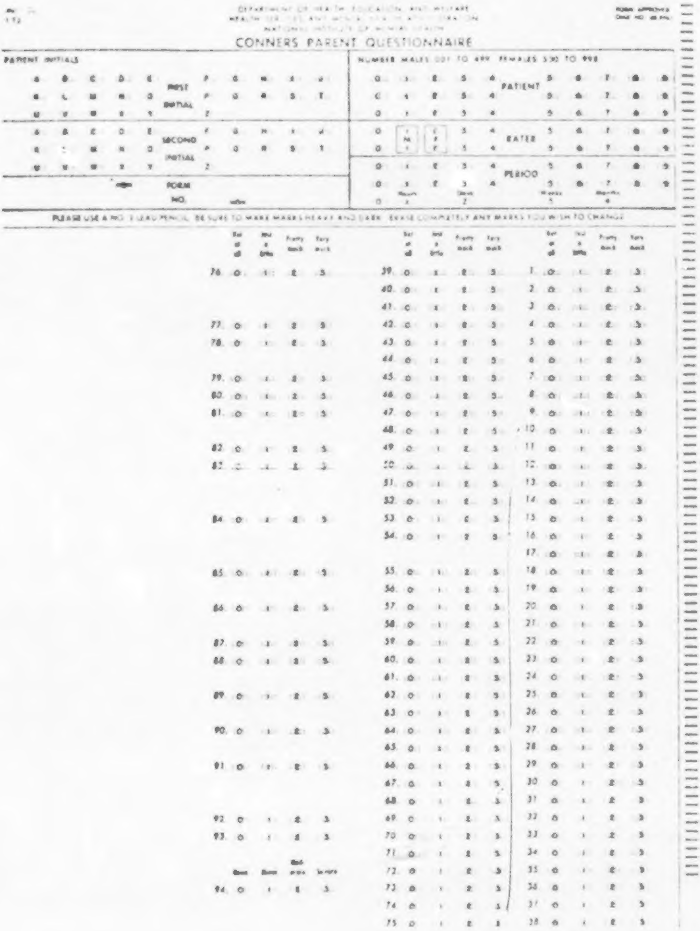
SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

OBSERVATION			Not at all	Just a little	Pretty much	Very much
PERFECTIONISM	76. Everything must be just so	76.	0	1	2	3
	77. Things must be done same way every time	77.	0	1	2	3
	78. Sets goals too high	78.	0	1	2	3
ADDITIONAL PROBLEMS	79. Inattentive, easily distracted	79.	0	1	2	3
	80. Fidgeting	80.	0	1	2	3
	81. Cannot be left alone	81.	0	1	2	3
	82. Climbing, gets into things	82.	0	1	2	3
	83. A very early riser	83.	0	1	2	3
	84. Will run around between mouthfuls at meals	84.	0	1	2	3
	85. Demands must be met immediately—easily frustrated	85.	0	1	2	3
	86. Cannot stand too much excitement	86.	0	1	2	3
	87. Laces and zippers are open	87.	0	1	2	3
	88. Cries	88.	0	1	2	3
	89. Unable to stop a repetitive activity	89.	0	1	2	3
	90. Acts as if driven by a motor	90.	0	1	2	3
	91. Mood changes quickly	91.	0	1	2	3
	92. Poorly aware of surroundings or time of day	92.	0	1	2	3
	93. Clumsy	93.	0	1	2	3

		None	Minor	Moderate	Severe
94. How serious a problem do you think your child has at this time?	94.	0	1	2	3

	Not at all	Just a little	Pretty much	Very much
39.	0	1	2	3
40.	0	1	2	3
41.	0	1	2	3
42.	0	1	2	3
43.	0	1	2	3
44.	0	1	2	3
45.	0	1	2	3
46.	0	1	2	3
47.	0	1	2	3
48.	0	1	2	3
49.	0	1	2	3
50.	0	1	2	3
51.	0	1	2	3
52.	0	1	2	3
53.	0	1	2	3
54.	0	1	2	3
55.	0	1	2	3
56.	0	1	2	3
57.	0	1	2	3
58.	0	1	2	3
59.	0	1	2	3
60.	0	1	2	3
61.	0	1	2	3
62.	0	1	2	3
63.	0	1	2	3
64.	0	1	2	3
65.	0	1	2	3
66.	0	1	2	3
67.	0	1	2	3
68.	0	1	2	3
69.	0	1	2	3
70.	0	1	2	3
71.	0	1	2	3
72.	0	1	2	3
73.	0	1	2	3
74.	0	1	2	3
75.	0	1	2	3

	Not at all	Just a little	Pretty much	Very much
1.	0	1	2	3
2.	0	1	2	3
3.	0	1	2	3
4.	0	1	2	3
5.	0	1	2	3
6.	0	1	2	3
7.	0	1	2	3
8.	0	1	2	3
9.	0	1	2	3
10.	0	1	2	3
11.	0	1	2	3
12.	0	1	2	3
13.	0	1	2	3
14.	0	1	2	3
15.	0	1	2	3
16.	0	1	2	3
17.	0	1	2	3
18.	0	1	2	3
19.	0	1	2	3
20.	0	1	2	3
21.	0	1	2	3
22.	0	1	2	3
23.	0	1	2	3
24.	0	1	2	3
25.	0	1	2	3
26.	0	1	2	3
27.	0	1	2	3
28.	0	1	2	3
29.	0	1	2	3
30.	0	1	2	3
31.	0	1	2	3
32.	0	1	2	3
33.	0	1	2	3
34.	0	1	2	3
35.	0	1	2	3
36.	0	1	2	3
37.	0	1	2	3
38.	0	1	2	3



DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

FORM APPROVED
OMB NO. [illegible]

CONNERS PARENT QUESTIONNAIRE

PATIENT INITIALS

FIRST INITIAL
A B C D E F G H I J
K L M N O P Q R S T
U V W X Y Z

SECOND INITIAL
A B C D E F G H I J
K L M N O P Q R S T
U V W X Y Z

FORM NO.

NUMBER MALES 001 TO 499 FEMALES 500 TO 998

PATIENT
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9

RATER
0 1 M 1 F 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9

PERIOD
0 1 2 3 4 5 6 7 8 9
0 1 2 3 4 5 6 7 8 9
0 Hours 1 Days 2 Weeks 3 Months 4

PLEASE USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

	Not at all	Just a little	Pretty much	Very much
76.	0	1	2	3
77.	0	1	2	3
78.	0	1	2	3
79.	0	1	2	3
80.	0	1	2	3
81.	0	1	2	3
82.	0	1	2	3
83.	0	1	2	3
84.	0	1	2	3
85.	0	1	2	3
86.	0	1	2	3
87.	0	1	2	3
88.	0	1	2	3
89.	0	1	2	3
90.	0	1	2	3
91.	0	1	2	3
92.	0	1	2	3
93.	0	1	2	3

	[illegible]	[illegible]	[illegible]	Severe
94.	0	1	2	3

	Not at all	Just a little	Pretty much	Very much
39.	0	1	2	3
40.	0	1	2	3
41.	0	1	2	3
42.	0	1	2	3
43.	0	1	2	3
44.	0	1	2	3
45.	0	1	2	3
46.	0	1	2	3
47.	0	1	2	3
48.	0	1	2	3
49.	0	1	2	3
50.	0	1	2	3
51.	0	1	2	3
52.	0	1	2	3
53.	0	1	2	3
54.	0	1	2	3
55.	0	1	2	3
56.	0	1	2	3
57.	0	1	2	3
58.	0	1	2	3
59.	0	1	2	3
60.	0	1	2	3
61.	0	1	2	3
62.	0	1	2	3
63.	0	1	2	3
64.	0	1	2	3
65.	0	1	2	3
66.	0	1	2	3
67.	0	1	2	3
68.	0	1	2	3
69.	0	1	2	3
70.	0	1	2	3
71.	0	1	2	3
72.	0	1	2	3
73.	0	1	2	3
74.	0	1	2	3
75.	0	1	2	3

	Not at all	Just a little	Pretty much	Very much
1.	0	1	2	3
2.	0	1	2	3
3.	0	1	2	3
4.	0	1	2	3
5.	0	1	2	3
6.	0	1	2	3
7.	0	1	2	3
8.	0	1	2	3
9.	0	1	2	3
10.	0	1	2	3
11.	0	1	2	3
12.	0	1	2	3
13.	0	1	2	3
14.	0	1	2	3
15.	0	1	2	3
16.	0	1	2	3
17.	0	1	2	3
18.	0	1	2	3
19.	0	1	2	3
20.	0	1	2	3
21.	0	1	2	3
22.	0	1	2	3
23.	0	1	2	3
24.	0	1	2	3
25.	0	1	2	3
26.	0	1	2	3
27.	0	1	2	3
28.	0	1	2	3
29.	0	1	2	3
30.	0	1	2	3
31.	0	1	2	3
32.	0	1	2	3
33.	0	1	2	3
34.	0	1	2	3
35.	0	1	2	3
36.	0	1	2	3
37.	0	1	2	3
38.	0	1	2	3

table. It is particularly necessary for the child to have a prolonged period when he is expected to sit still some way from the examiner in order to provide an opportunity for hyperactive or disinhibited behaviour to be readily observable, if it occurs. The room should be arranged so that the toy gun, paper and pencils, kaleidoscope, some coloured beads and a string and some match puzzles are situated so that the child can see them but not reach them without moving. As far as possible the rest of the room should be free of toys or other distracting objects.

The first part of the interview is unstructured; the aim is to get the child relaxed and talking freely, to assess the relationship he is able to form in such a setting, the level and lability of his mood, his conversational speech and any habitual mannerisms. In order to provide an adequate sample of behaviour it is necessary to allow at least 15 minutes for unstructured conversation with the child on the lines suggested.

The child should be encouraged to talk about recent events and activities, what sort of things he likes doing after school and at weekends, what he does with his friends and with his family, the games he plays and the things he is interested in, what he enjoys and what he does not enjoy at school, etc. He may also be asked about his hopes for the future—such as what he wants to do when he leaves school or when he is grown up, but in this diagnostic interview there is no need to explore the child's fantasy life.

The interviewer should respond with interest, concern or enthusiasm as may be appropriate (to set a relaxed and informal atmosphere, to try to elicit a range of emotions in the child, to assess the emotional responsiveness of the child and the kind of relationship he forms with the examiner[1]. The interview must be geared to the child's age, intelligence and interests, and the examiner must react naturally to what the child says and does. If the emotional responsiveness of the child is to be adequately assessed it is necessary for the examiner himself to show a range of emotions (being more serious or concerned when asking about feelings of distress or worry and more lively when responding to the child's account of what interests or amuses him). The interview must *not* be conducted in a rigid manner as if following a questionnaire; it is essential for the examiner to show interest (by smiling, leaning forward, etc.) and to respond appropriately to what the child says and does.

All children should also be asked if they have any friends, the names of their friends, what they do with them and how they get on with other children at school and at home. They must also be asked:

"Do you ever feel lonely?"

"Do you get into fights sometimes?"

"Do you ever get teased?" and

"Do other children ever pick on you?"

If the child says that he is bullied or picked on he should be asked if he thinks that he is picked on more than most other children. He should also be asked why he thinks he is picked on. In the same sort of way he should be asked how he gets on with his brothers and sisters. If the child says he gets into fights he should be asked if he likes fighting, whether they are "friendly" fights or "real" fights, who he fights and how often he fights.

In addition to this rather general approach, all children must be asked specifically about worries, fears, unhappiness and bad dreams, using the following questions (not necessarily in this order):

"Most people have some things that they worry about. What kind of things do you worry about? . . . Do you ever lie awake at night worrying about things? . . . Does thinking about nasty things ever stop you from getting to sleep? . . . Do you ever get nasty thoughts on your mind that you cannot get rid of?"

"Do you get fed up sometimes? . . . or feel miserable? . . . or do you cry sometimes? . . . do you ever feel really unhappy?"

"Lots of children have things they are afraid of—such as spiders or shadows at night. Do you ever get afraid of things—like being afraid of the dark? . . . or of dogs or cats? . . . or of other things?"

"Do you ever dream? . . . What about bad dreams or nasty dreams? . . . or nightmares?"

"Many people have got some things that tend to make them really angry. What kind of things make *you* get angry and annoyed?"

The general form of wording suggested above should be followed as closely as possible, but the questions should be put in an informal conversational manner using terms appropriate to the age, sex and social background of the child.

If the children do not understand the questions, the examiner should re-word or explain as necessary. If anything positive comes up either in answer to these questions or elsewhere in the interview, the examiner should probe regarding the severity, frequency, and setting of the emotions ("Do you ever feel so miserable that you want to go away and hide? . . . or that you want to run away? . . . How often do you feel like that? . . . What sort of things seem to make you feel fed up? . . . Do you feel like that at home, at school, etc.?") The answers to the questions may be important, but the emotions they provoke are of greater interest. Children will often produce answers they think you want, but the anxious or depressed child can usually be distinguished by his affective state when talking about worries, fears, feeling fed-up, etc. If the child reports any fears, he should be asked what he does when he meets whatever it is he is afraid of (e.g. if he is afraid of dogs—does he cross over the road if he sees a dog coming towards him on the pavement, does he scream, does he run away, what if it is a friendly dog or a puppy). It may also be useful to get the child to imagine the situation (e.g. if he is afraid of spiders—suppose there was a spider crawling down the curtain over there and coming across the floor there towards your chair and near to your feet, etc.). All children must be asked these questions, but much of the interview must also consist of neutral or cheerful topics. Preoccupation with anxious or depressive topics should be judged on how far the child *spontaneously* extends answers to these questions or brings up similar material in other parts of the interview. Note that "preoccupation" can *only* be rated if the child either makes *spontaneous* remarks about anxious or depressive topics or *extends* answers on these topics *beyond* what was required by the question. Whether the topic is anxious or depressive is judged on the content of the topic and the child's expressed feelings about the topic.

The child should be asked to draw a man and should be encouraged to tell you what he has drawn.

In order to assess attention span, persistence and distractibility, the child must be given some tasks. These must be within his ability but should be near enough to his limits in order to test his persistence, etc. (not his cognitive abilities). Drawing a man constitutes one task, but in addition children may be asked to give the days of the week forward and backwards, the months of the year, and also do some simple arithmetic (this might include serial 7s from 100, serial 3s from 20, addition, subtraction, multiplication, or multiplication tables). To rate persistence it is necessary to find some task near the limit of the child's capacity and so requiring persistence for its completion. The suggestions above are only meant to be a general guide.

For distractibility the examiner should note the child's response to all visual, tactile, auditory and other stimuli present at interview (objects in the room, noises outside, lights, etc.). In addition, the examiner should provide the additional stimuli of (*a*) coughing, (*b*) tapping on the desk with a pencil and (*c*) moving about in the chair and then getting up and walking about, when the child is engaged in a task (such as drawing). These stimuli should be repeated several times to assess the child's response first time and on subsequent occasions. It is usual for distractibility to be more easily rateable on the basis of the child's reactions to extraneous stimuli throughout the whole interview than on the specific responses to the standard stimuli. Most children have negligible discernible reaction, or none, to the standard stimuli.

The extent to which the child startles or "jumps" to sudden extraneous noises or to sudden movements by the examiner should be observed. To assess startle the examiner must also make a loud noise by dropping a book or metal ashtray on the floor close to the child when the child is drawing.

Ratings 1 to 10 of the schedule* are "peak" ratings—i.e. the maximum abnormality shown by the child at any part of the interview is rated. The remainder of the scales (11–31) are overall ratings to be made on a general assessment of the child's behaviour throughout the whole interview.

It is important to differentiate tension, mannerisms and fidgetiness. "Tension" refers only to *muscle* tension at rest, and it is usually evident by clenching of the jaws, sitting stiffly on the edge of the chair, gripping of the sides of the chair or table, or grasping the hands tightly together. Mannerisms are confined to movements which are both repetitive and stereotyped. Fidgetiness concerns other extraneous movements such as twisting about in the chair or fiddling with things.

Gross activity level ratings should follow the rating instructions. Note that the rating (apart from point 9) refers to activity *relative* to the situation of the interview, and children who get up and move about may merely be disinhibited or be disregarding the examiner or the situation. They are not necessarily hyperkinetic in the strict sense.

Observed anxiety must not be rated on inference from non-anxious items. For example, the fact that the child is not very easy to get to know or is overactive is not relevant for the rating of anxiety.

Emotional responsiveness refers to the child's emotional responsiveness *to the interviewer*. The child should show an appropriate range of emotions in response to the interviewer's talk and behaviour in order to rate "O".

Spontaneous comments should be noted *as they occur* rather than at the end of the interview.

It is particularly important that every effort be made to avoid "halo" effects. Each item should be rated without regard to any other ratings.

On the front page of the coding schedule there is a space for a free description of the child and his behaviour at interview. The examiner should describe as fully as possible the course of the interview, the child's behaviour and reactions. The codings take account of ratings on most of the main categories of observable behaviour, but the free description should add "flesh" to the codings by providing a vivid picture of the patient and his conduct during the examination. It should include some account of the content of the child's speech.

In making the final evaluation of psychiatric state, the examiner should use all relevant data observed in the child or reported by him. The nature of the psychiatric disorder and the evidence for it should always be specified.

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* Interested research workers can obtain copies of the schedule from the authors.

Michael Rutter, M.D., M.R.C.P., D.P.M., *Senior Lecturer, Institute of Psychiatry, and Honorary Consultant Physician*
Philip Graham, M.A., M.R.C.P., D.P.M., *Research Worker, Institute of Psychiatry, and Consultant Physician*
The Maudsley Hospital, London, S.E.5

(*Received 15 May, 1967*)

SCORED NEUROLOGICAL EXAMINATION*

John Close, M.D.**

I. Introduction

This Scored Neurological Examination is designed to assist the observer in determining whether neurological soft signs are present in a child. Because this is not a test of learning, it is important that the patient fully understand what is expected of him. The examiner (who need not necessarily be a physician) should demonstrate every task to be performed while giving the verbal instructions in the test description. Instructions given before the test should be used in an identical manner from one child to the next utilizing a set routine of presentation. The time usually required to perform this test is 15 to 20 minutes.

At the beginning of testing, the child's attention should be obtained by making the statement, "Pay attention and watch what I do because you will have to do it after me." Since many items require stopwatch timing, the caution, "Don't start until I say *NOW*, okay?" must be given immediately after the description and demonstration of each task. Proper instruction and clear demonstration are important contributions to the effectiveness of this scored examination.

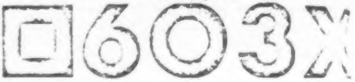
A positive atmosphere should be maintained throughout the examination, accompanied by verbal praise and reinforcement. Incentive, such as the promise of [illegible] of a toy from a box of inexpensive toys [illegible] be used upon completion of testing.

II. Mate[illegible]nd Equipment

The room used for the test should be adequately lighted, have a minimum noise level, and be as free as possible of extraneous materials. One wall should be darkened by a black felt cloth or blackboard to provide a background for the test of opticokinesia. Other needed items include the examiner's chair (facing away from the dark wall), a chair for the patient which faces a table or desk, and a convenient for examining materials. Adhesive tape, $1\frac{1}{2}$ in width, should be used to make a six-foot straig on the floor away from any nearby obstructions.

The following materials are needed:

a. A standard lined $8\frac{1}{2}$ x 11-inch writin Clearly inked geometrically attractive of a square, a six, a circle, a three, and (approximately one inch high) should be on the cardboard back of the pad.



b. Three or four sharp, soft lead pencils.
c. A ball point pen.
d. A toy cricket or other hand-held device for ing clicking noises.
e. A stopwatch (expensive models are unne sary).
f. A two-point discriminator with one-centim separation.
g. A ring (simple wedding band type).
h. A car key.
i. A coin (nickel).
j. A standard two-inch safety pin.
k. A box of small, cheap toys.

III. Administration and Scoring

Rapport should be established by a few minute conversation. Acclimatization to test circumsta may then be phased in by one or two simple scored tasks, such as, "Can you show me your foot? Good! Now point to your left ear." (G correction is used with an incorrect gesture, and the question repeated.) Above all, a completely couraging, nonpunitive atmosphere is required.

In all the directions that follow, quotation m indicate verbal instructions and parentheses enclo physical description of the demonstration. Right left-handedness should be recorded before the begins.

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*The neurological examination and instructions were compiled from diverse sources by the author.

**Abbott Laboratories, North Chicago, Illinois.

Questions 1–20

For Questions 1–8:

1. Finger to Nose

"I want you to touch a finger to your nose. Begin with your arm out here."

(Extend the arm laterally with the hand in a loose fist, index finger extended as pointer.)

"Now do like this."

(Make a wide sweep medially to touch the nose.)

Score: 1—Smoothly and accurately performed.
2—Slowly, jerkily, and missing the target, then correcting. (If 10 seconds pass with no attempt, instruct and demonstrate again.)
3—Same as 2; but correcting only after encouragement or a repeat instruction and demonstration.
4—Same as 3; but without correcting target error.

If the child simply does not do the test, no score is given; instead, a straight line is drawn across the four scoring blanks.

2. Contralateral Finger to Nose

"Now do the other hand."

(Demonstrate again.)

3. Finger to Nose, Eyes Closed

"Now close your eyes and do that again."

(No demonstration necessary.)

Score as in Test No. 1.

4. Contralateral Finger to Nose, With Eyes Closed

"Close your eyes again and do it with the other hand."

(No demonstration necessary.)

Score as in Test No. 1.

5. Heel to Shin

"Touch your heel against the front of your other leg, up high like this."

(Demonstrate the heel touching just beneath the patella.)

Score as in Test No. 1.

The use of either foot is acceptable.

6. Contralateral Heel to Shin

"Now do it with the other heel."

(Demonstrate again.)

Score as in Test No. 1.

7. Heel to Shin, Eyes Closed

"Now close your eyes and do that last one again."

(No demonstration necessary.)

Score as in Test No. 1.

8. Contralateral Heel to Shin, Eyes Closed

"Now close your eyes and try it with the other heel."

(No demonstration necessary.)

Score as in Test No. 1.

For Questions 9–16: The child is told to turn to the table where a sheet of paper from the pad is placed in front of him and the date written in the upper right-hand margin. Tape or thumbtacks may be used to fix the page securely in front of the child. The child is then given a pencil and told to write or print his name at the upper left. No matter how poorly this is performed, the child should be told that it is well done.

For drawing on the palm of the child's hand, the tester should try to imagine a frame that consists of a line bordering one-half inch within the proximal, distal, and lateral margins of the hand. All numbers and figures should be drawn in the palm from left to right as in a book. The non-writing end of the ball point pen should be used. On all graphesthesia and stereognostic samples the child should be told, "Now turn your face up toward the ceiling and close your eyes." One must be certain that the demonstration cannot actually be seen. Having been told this, take the palm of the child's hand in your hand and slowly (about three seconds) and smoothly draw a number or figure, the base of which should be at the thenar and hypothenar portions of the palm. The child should then be told, "Open your eyes and draw the figure on the paper." Repeat the demonstration one or more times with each hand until the child understands the procedure. The actual examinations are then started.

The child is told, "Draw on the paper each of the things I draw in your hands while your eyes are closed. I may draw another number or I may draw figures like a circle or square."

9–16 Graphesthesia

"Now turn your face up and close your eyes while I draw. There. Now open your eyes and see if you can draw it."

(9. Draw a square—right hand)
(10. Draw an x—left hand)
(11. Draw a circle—right hand)
(12. Draw a square—left hand)
(13. Draw an x—right hand)

The same verbal instructions are used prior to each of the tasks listed to the right.

(14. Draw a 3—left hand)

(15. Draw a circle—right hand)

(16. Draw a 3—right hand)

If the child is unsuccessful after the first tracing, make the remark, "That's fine, close your eyes and let me do it again." If after the second time the child is still unable to draw the figure, raise the pad off the table so that the figures drawn on the back are visible. "Can you pick out the one I drew? Fine, draw it." The child is allowed to draw the figure while still visualizing the example on the back of the pad.

Scoring: The 1 column is checked if the child does the figure correctly after the first trial.
The 2 is checked if the child does it successfully after the second example.
The 3 is checked if the child picks it from those drawn on the pad.
The 4 is checked if the child is still unsuccessful after two examples and the visualization of the figure on the pad.

Questions 17–20 involve stereognosis. Different objects are placed in the hands without bilateral repetition of the same object. The method of testing and of scoring here is similar to that in the preceding description. The child's face should be directed toward the ceiling with eyes closed at all times when the objects might be in sight. The box of objects is kept beneath the table out of sight. Each object is placed in the child's hand in the order described on the examination form for a period of approximately five seconds, and then the child is told, "Now give it back. Without looking, tell me what it is." If at that point the child is unable to identify the object, it is replaced in the hand with the remark, "Feel it and think what it could be." After five seconds, it is removed and replaced in the box with the other objects. If the child is still unable to identify it, the box is brought into sight with the question, "Can you pick it out of here?"

Scoring: 1 is checked if the child names the object successfully on the first trial.
2 is checked if the child names the object after the second placement in the hand.
3 is checked if the child is successful only after seeing the object.
4 is checked if the child is unable to pick the object out of the box.

B. Questions 21–29

Here, the straight line (represented by tape on the floor) is used for testing. As long as the patient's foot is touching the tape in an while walking the line, it is not considered a

21. Walking Tiptoe
"Walk this line to the end up on your
(Demonstrate while up on the balls of the arms hanging naturally, carefully walk line.)
"Be sure you stay on the line."
The examiner should wait at the end of line. This serves two purposes: First, he mains close to the child to protect a falling; and secondly, he will be posit for the next demonstration, the return An error count is made f each time child misses the line or puts a foot down footed. This actual count, 0, 1, 2, or 3 scored in the appropriate column. If a grea number than 3 occurs, 3 is scored and actual number recorded in the far ri margin.

22. Heel Walking
"Now go back on your heels like this."
(Arms at side, walk on heels on the line.)
Score: The same method as in Test No. 21 used.

23. Hopping on One Foot
"Can you hop all the way without missing th line? Be sure not to put the other foot down
(Demonstrate a hop on the line.)
The examiner should again remain at the e of the line.
Scoring: An error occurs if the child miss the line or if the elevated foot allowed to touch the floor.

24. Hopping on the Other Foot
"Now hop back on the other foot."
(Demonstrate accordingly.)
Score as in Test No. 23.

25. Tandem Walking Forward
"Now be sure you put your heel against you toe and walk to the end staying on the line
(Demonstrate heel-toe walking on line an remain at the end.)
Score: An error consists of not placing th heel to toe or missing the line completely.

26. Tandem Walking Backward
"Now do the same thing backwards."
(Demonstrate accordingly.)
Score as in Test No. 25.

For Question Nos. 27, 28, and 29, the child seated at the side of the table with hands

Three clear examples are given in each before actual counting begins. The examples ld always be given exactly the same way. The should be performed on the dominant side; in ght-handed child the right cheek and right d should be employed. Again, the child's face rected upward with the eyes tightly closed.

Face-Hand Test

"I am going to brush your hand and face at the same time."

(With a light fluff of cotton in each hand, the dorsum of the hand and the cheek beneath the malar eminence should be brushed simultaneously and softly with as nearly equal pressure as is possible.)

"Did you feel it?"

"Now I'm going to brush only your face."

(This is then performed.)

"Did you feel it?"

On the third example, the hand only is brushed, and again with the forewarning:

"Now I'm going to brush only your hand."

(This is then performed)

Begin actual test—

"Now I'm going to do this some more and I want you to tell me what I do each time."

(First, hand only; Second, face only; Third, face-hand combination; each time asking the child: "There, what did I do?")

Scoring If the child misses none of these, the 0 column is checked; if he misses one, the column 1 is checked; and so on up to a total of missing all three.

Face-Noise Test

This test is similar, except that the face is brushed at the same time a cricket toy is clicked in the ipsilateral ear. Again, three variations are performed as examples. First, the cricket only is clicked; second, the cricket is clicked and the face is brushed; third, the cricket is clicked without brushing the face. Note that the cricket is clicked in every example.

Begin actual test—

(First, the cricket is clicked and face simultaneously brushed;

"Can you tell me what I did?"

Second, the cricket is clicked without brushing;

"Can you tell me what I did?"

Third, the cricket is clicked and face brushed again.

"Can you tell me what I did?"

Scoring: As in the case of Test No. 27, the number of errors is counted; if the child misses none of the trials, a 0 is checked, if one of the examples is missed, a 1 is checked; if two are missed, the 2 is checked; and if all three are missed, the 3 is checked.

29. Two-Point Discrimination

Again, three examples are given utilizing the one-centimeter separation, two-point discriminator on the pad of the digiti minimi.

"You see, I have only touched you with one point."

(Only one point is touched.)

"I used two points on you that time, could you tell it?"

(Both points are used.)

"Now only one point again."

(One point only is again used.)

Begin actual test—

"What did I do that time?"

(Using two points.)

"What did I do that time?"

(Using one point.)

"What did I do that time?

(Using two points.)

Scoring: Same as in Tests 27 and 28, appropriate column is checked for 0 through 3 errors.

C. Questions 30–36

These tests require the use of a stopwatch and accurate timing of the child's performance. It is necessary that the child know clearly when the test starts and that he is told to keep doing the task until the examiner tells him to stop. For scoring purposes, if the child persists in the task for 20 seconds or more, the first column is checked; 15 to 19 seconds, the second column is checked; 10 to 14 seconds, the third column is checked; and 0 to 9 seconds, the fourth column is checked. At the outset of these tests, the child is told, "Now I am going to tell you some things to do; be sure that you don't start doing any one of them until I say, 'begin.' Do you understand? Also, be sure you continue doing them until I tell you to stop."

30. Tongue Extrusion

"Watch me now."

(The examiner should stick out his tongue for a period of 3–4 seconds.)

"Did you see what I did? All right, now when

I tell you to start do it a long time until I tell you to stop. Ready—begin!"

31. Arms Extended

"Hold your arms in front of you like this until I tell you to stop."

(The arms should be extended directly in front of the examiner, palms down.)

"Could you see how I did that? Are you ready to start? All right—begin!"

Presence of drift does not alter the timed nature of scoring in this task.

32. Eyes Closed

"Watch how tightly I can close my eyes."

(Close the eyes very tightly.)

Now you do it when I tell you to. Ready—begin!"

33. Stand on One Foot

"Now I'm going to stand on one foot without moving it."

(Stand up on either foot with the arms hanging down naturally at the sides.)

"It doesn't matter which foot you stand on. Did you see how I did that? Are you ready? Begin!"

34. Stand on the Other Foot

"Now do the same thing when I tell you to start, standing on the other foot. Are you ready? Begin!"

(No demonstration necessary.)

35. Romberg

"Now stand up like this on both feet but keep your eyes closed."

(The examiner stands in front of the child on both feet, erectly, with his hands at his sides and his eyes tightly closed.)

"Are you ready to do that? All right, begin!"

36. Tandem Romberg

"Now put one heel against the other toe and stand with your eyes closed until I tell you to stop. Either foot may be in front."

(Demonstrate eyes closed, tandem stance, a
at sides.)

D. Questions 37–43

In these tests, the examiner should assure himself of exactly what constitutes a four-per-second beat. A general tendency is to make this beat faster than it should be. The examiner should appraise his own sense of rhythm by listening to a four-per-second example; either with a clock or, if available, a metronome. A typical alarm clock or wrist watch (but not a stopwatch) ticks at a four-per-second rate.

Each test is of five seconds' duration. Th
is seated at the table facing the dark back
wall, and the examiner's demonstrations sh
clear and perhaps exaggerated. The child
be allowed three or four seconds' practic
Nos. 37, 39, 41, and 43. If a mistake is
which the child would be downgraded, such
lack of smooth delivery, the child should
formed. He should also be told at the out
to move the rest of his body but rather
part that is supposed to be moving. Advent
movement will be considered as any moveme
necessary to the task at hand, whether it
ments, such as, a jerk, twitch, grimace, bod
tortion, or sticking out of the tongue. Cont
rigidity is not considered adventitious. Th
ing point of each of these tasks for the pur
timing should be a clear-cut signal.

37. Finger Tapping

"Now watch how I tap only my finger
this fast. Notice that I leave my other
down at my side."

(Demonstrate sitting erectly with the ta
motion mainly comprised of finger acti
hand motion.)

"You see that I am just moving my finge
not my hand and arm? Would you
practice that quickly before we start?"
At this point, if the child is going too
he should be told, "Go a little faster."
allowed to practice again.

"That looks good. Are you ready now
right, begin."

Scoring: The examiner is actually
three things at once. A brief
larization and practice are ne
accomplish this. The first ty
scoring is the actual count
number of taps performed
five-second period. The child
be shown the proper rate of
at the beginning. The numb
taps is scored in the proper
by a *checkmark* (✓). Sim
ously, one is making mental
adventitious movements. Th
ber represents a separate
is indicated by a *circle* (○)
proper column.
"Quality" is also scored one
four; the examiner writing
propriate number based on

judgment of performance. This evaluation is not meant to reflect absolutely correct rhythmicity, but rather the smoothness of overall delivery. Points should not be taken away if the child ends the task at a more rapid or slower tapping rate than that with which he began, as long as he phases in and out of such changes smoothly. We downgrade the child for sporadicity or for the appearance of "bursts" in his sequencing. If the child only makes one such change in rhythm, he will receive a score of 1 in the quality column; if he makes this error twice, he will receive a score of 2; three times, a score of 3; and a score of 4 could represent a completely arrhythmic performance.

38. Finger Tapping—Other Hand

"Now we are going to do it with the other hand; why don't you practice that for a moment."

(No repeat demonstration necessary.)

"That's fine. Are you ready now? Begin."

Scoring as in Test No. 37

39. Foot Tapping

"Now watch how I sit and tap only my foot just this fast. Would you like to practice that for a moment?"

(Demonstrate accordingly. The heel remains on the floor. Assure that there is moderate extension at the knee or the resultant angle on the foot makes the task difficult.)

"That's fine. Are you ready now? Begin."

Scoring as in Test No. 37

40. Foot Tapping—Other Foot

"Now let's do it with the other foot; you may practice for a moment."

(No repeat demonstration necessary.)

Scoring as in Test No. 37

41. Finger and Foot Synchronization

"Now we are going to try the finger and the foot at the same time. You must tap them together at the same rate you have been tapping them separately. Watch how I do it."

(Examiner must be careful to synchronize finger and foot tapping through several repetitions at an adequately fast rate. Like sides are always paired: right hand with right foot; left hand with left foot.)

"Do you want to practice that now?"

"That's fine, do you think you are ready to start? All right. Begin."

Scoring: The scoring of tap count and adventitious movement count is the same here as in previous examples. However, the "Quality" column score now reflects the actual number of times the child deviates from synchronized tapping. A complication of this scoring immediately becomes obvious; that is, if the child is unsynchronized from the start. In such a circumstance, one must grade quality according to the amount of time during the test that asynchrony is apparent. A quality score of 1 is well synchronized, hand and foot, through the entire study. If the child is not well-synchronized for some portion of the test, divide total test time into thirds. If the child's tapping is not synchronized for one-third of the time, a quality score of 2 is recorded; if two-thirds of the time asynchrony is demonstrated, a score of 3 is received; and a quality score of 4 is recorded for gross asynchrony throughout.

42. Synchronous Finger and Foot Tapping—the Opposite Side

"Now I want you to tap your foot and finger on the other side together. Do you want to practice that? All right, begin."

(No repeat demonstration necessary.)

Scoring as in Test No. 41

43. String Test

This is an opticokinetic test performed with a rapid and a slow component. An object on the examiner's hand should serve as a target on which the child may fix his gaze; a ring on a finger or a piece of chalk between fingers is adequate. The motion is made against the dark background and through a distance of about two feet. The test hand is moved away from the body rather quickly, then brought back to the examiner's side more slowly. It is performed approximately two feet from the child with first the right and then the left hand. The examiner should step to the right or left far enough so that the demonstrating hand will be directly in front of the child's face. The child's head must remain still, following only with the eyes.

"Now I'm going to pretend that I am pulling several times on a piece of string that is hooked to my belt. I want you to follow my hand with your eyes everywhere it moves. But you can't move your head. It may help you if you watch this ring on my finger."

(The hand is moved away from the body in a quick motion and then more slowly brought back medially. This is done five cons times rhythmically.)

"Now I'm going to do it on the other

It is permissible for the examiner to pl hand on the child's head, if it would he stabilize him. The number of times the p successfully follows the target movemen of the possible five is circled. If nystagm present, the direction of the fast compo should be indicated.

ABBOTT USE ONLY

SCORED NEUROLOGICAL EXAM

Patient Name ______________________________

INSTRUCTIONS A score of one to four is possible on each category; from left to right ALWAYS indicates from good to poor. Methods for scoring are indicated; if questions arise, consult the discussion section on the neurological exam. Demonstrate each.

Score The Following: 1 - performed correctly 3 - performed poorly or only after repeat instruction and demonstration

2 - performed but not well 4 - Unsuccessful even after repeated demonstration

			1	2	3	4
	1. Touch your finger to your nose					
	2. Touch your other finger to your nose					
	3. Close your eyes and touch your finger to your nose					
	4. Close your eyes and touch your other finger to your nose					
	5. Touch one heel to your other leg					
	6. Do the same with your other heel					
	7. Close your eyes and do it again					
	8. Now the other heel					
Child writes name at the top of paper Trace a "6" in each palm and identify it for the child Figure is drawn in palm as child would see it "Close your eyes and when I draw a mark on your hand. Now open your eyes and draw it on paper." (Attach child's paper)	9. □	Right Hand				
	10. X	Left Hand				
	11. O	Right Hand				
	12. □	Left Hand				
	13. X	Right Hand				
	14. 3	Left Hand				
	15. O	Right Hand				
	16. 3	Left Hand				
"Close your eyes and tell me what I'm putting in your hand."	17. Coin	Right Hand				
	18. Ring	Left Hand				
	19. Safety Pin	Right Hand				
	20. Key	Left Hand				

		0	1	2	3
SCORING Count number of errors (More than 3 scored as three) An error is definite deviation from the line or steps incorrectly done	21. Walk the line to the end on your toes				
	22. Walk back on your heels				
	23. Hop on one foot to the end of the line				
	24. Now hop back on the other foot				
	25. Walk to the end this way (show tandem)				
	26. Now walk backwards the same way (6 steps)				
27. FACE-HAND	Brush face and/or hand gently with equal stroke (patient's eyes closed). Do three variations for grasp of the idea, then score total errors on the next three.				
28. FACE-NOISE	Brush face and/or click toy cricket ipsilateral ear (patient's eyes closed). Do three variations for grasp of idea, then score total errors on next three.				
29. Two point discrimination	1 cm. separation, dorsum of digiti minimi. Three variations to grasp the idea, then score total errors on next three				

PERSISTENCE MEASUREMENTS Period of uninterrupted success (stopwatch)	20 SEC	15-19 SEC	10-14 SEC	0-9 SEC
30. Stick out your tongue until I tell you to stop.				
31. Raise your arms out in front of you until I tell you to stop. If drift is present, indicate direction				
32. Close your eyes until I tell you to open them.				
33. Stand on one foot until I tell you to stop.				
34. Now stand on the other.				
35. Close your eyes and stand still until I tell you to stop. Tendency to fall? ( ) Yes ( ) No Direction?				
36. Now do it again like this. (Demonstrate tandem) Tendency to fall? ( ) Yes ( ) No Direction?				

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SCORING These are 5 second tests. Always demonstrate with a 4/second beat. These scores are recorded for each: (1) Total taps (0-20) indicate with a checkmark (✓). (2) Total adventitious body movements - greater than 4 recorded as 4 - marked by a circle (0). (3) Quality of tapping (your best estimate, written in the box to the right of the columns.)

	NO. TAPS (✓) NO. MVMTS (0)	20 1	15-19 2	10-14 3	0-9 4	Quality
37. Demonstrate. Tap this fast with your finger; left						
38. right						
39. Demonstrate: Tap this fast with your foot; left						
40. right						
41. Demonstrate: Tap with your fingers and foot; left						
42. right						
43. String test. Circle the number of times child successfully followed the five motions: Remark on any nystagmus	to the left to the right	5 5	4 4	3 3	2 2	1 1

Comments ____

____

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____

____

____

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________________________   ________________

Signature   Date Signed

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
HEALTH SERVICES AND MENTAL HEALTH ADMINISTRATION
NATIONAL INSTITUTE OF MENTAL HEALTH

PHYSICAL AND NEUROLOGICAL EXAMINATION FOR SOFT SIGNS

The Physical and Neurological Examination for Soft Signs (MH-9-41 PANESS) is a 4 page form for the assessment of physical status (pages 1 and 2) and soft neurological signs (pages 3 and 4) in pediatric populations. *BEFORE ATTEMPTING TO COMPLETE THE FORMS, RATERS SHOULD BE FAMILIAR WITH THE INSTRUCTIONS GIVEN IN THE ECDEU ASSESSMENT MANUAL. THIS IS PARTICULARLY CRUCIAL FOR THE EXAMINATION OF SOFT NEUROLOGICAL SIGNS.*

The neurological examination for soft signs has been developed and copyrighted by Abbott Laboratories and their permission to use it is gratefully acknowledged.

IMPORTANT – PLEASE READ CAREFULLY BEFORE MARKING THIS FORM.

INSTRUCTIONS FOR COMPLETION OF MULTIPLE PAGE FORMS

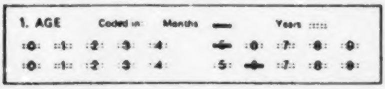
1. Complete page 1.
2. Following completion of page 1 carefully tear out and remove the pink protective sheet lying between the carbon and your copy of page 2. Follow this procedure for each subsequent page. You must do this to obtain a copy of the data for your files.

   CAUTION: DO NOT REMOVE PINK PROTECTIVE SHEETS OTHER THAN THE ONE LYING BETWEEN CARBON AND COPY OF THE PAGE YOU ARE ABOUT TO COMPLETE.
3. When you have completed all pages of the form, carefully tear out and remove carbon papers and your copy pages. The machine scannable pages should be left in booklet form for shipment to the Biometric Laboratory in packages prepared according to instructions received from the Biometric Laboratory.

MARKING INSTRUCTIONS

Read each item and its numbered responses. When you have decided which response is correct, blacken the corresponding space on the page with a No. 2 pencil. Do not use a ball point pen. Make your mark as long as the pair of lines, and completely fill the area between the pair of lines. If you change your mind, erase your first mark COMPLETELY.

EXAMPLE: The child is 56 months old. Code as follows:

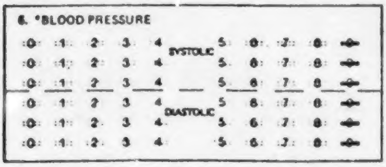


1. AGE Coded in: Months ▬ Years :::::

0	1	2	3	4	▬	6	7	8	9
0	1	2	3	4	5	▬	7	8	9

Mark a field of 9's if an item is unanswered or Not Ascertained.

EXAMPLE: Blood pressure was not taken; the rater codes as follows:



6. *BLOOD PRESSURE

0	1	2	3	4	SYSTOLIC	5	6	7	8	▬
0	1	2	3	4		5	6	7	8	▬
0	1	2	3	4		5	6	7	8	▬
0	1	2	3	4	DIASTOLIC	5	6	7	8	▬
0	1	2	3	4		5	6	7	8	▬
0	1	2	3	4		5	6	7	8	▬

MH-9-41 (1-73)

MH 9-61
1-73

NATIONAL INSTITUTE OF MENTAL HEALTH

FORM APPROVED
BUDGET BUREAU NO. [illegible]

PHYSICAL AND NEUROLOGIC EXAMINATION FOR SOFT SIGNS

PAGE 1

PATIENT INITIALS

FIRST INITIAL
A B C D E F G H I J
K L M N O P Q R S T
U V W X Y Z

SECOND INITIAL
A B C D E F G H I J
K L M N O P Q R S T
U V W X Y Z

FORM NUMBER

NUMBER MALES 001-499 FEMALES 500-999

PATIENT
0 1 2 3 4 5 6 7 8 9

RATER
0 1 2 3 4 5 6 7 8 9

PERIOD
0 1 2 3 4 5 6 7 8 9
Hours 1 Days 2 Weeks 3 Months 4

PLEASE USE A NO. 2 PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

1. AGE Coded in Months ☐ Years ☐
0 1 2 3 4 5 6 7 8 9

2. *HEIGHT Coded in Inches ☐ Centimeters ☐
0 1 2 3 4 5 6 7 8 9

3. *WEIGHT Coded in Lbs ☐ Kg ☐
0 1 2 3 4 5 6 7 8 9

4. *HEAD CIRCUMFERENCE Inches ☐ Cm ☐
0 1 2 3 4 5 6 7 8 9

5. *PULSE Code Per minute
0 1 2 3 4 5 6 7 8 9
Regular 0 Irregular 1

6. *BLOOD PRESSURE
SYSTOLIC 0 1 2 3 4 5 6 7 8 9
DIASTOLIC 0 1 2 3 4 5 6 7 8 9

7. *VISUAL ACUITY Code numerator only
RIGHT 0 1 2 3 4 5 6 7 8 9
LEFT 0 1 2 3 4 5 6 7 8 9

	Normal	Abnormal	NA
8. *OPHTHALMOSCOPIC	0	1	2
9. *AUDIOGRAM	0	1	2

	Right	Left	Mixed	NA
*HANDEDNESS	1	2	3	4

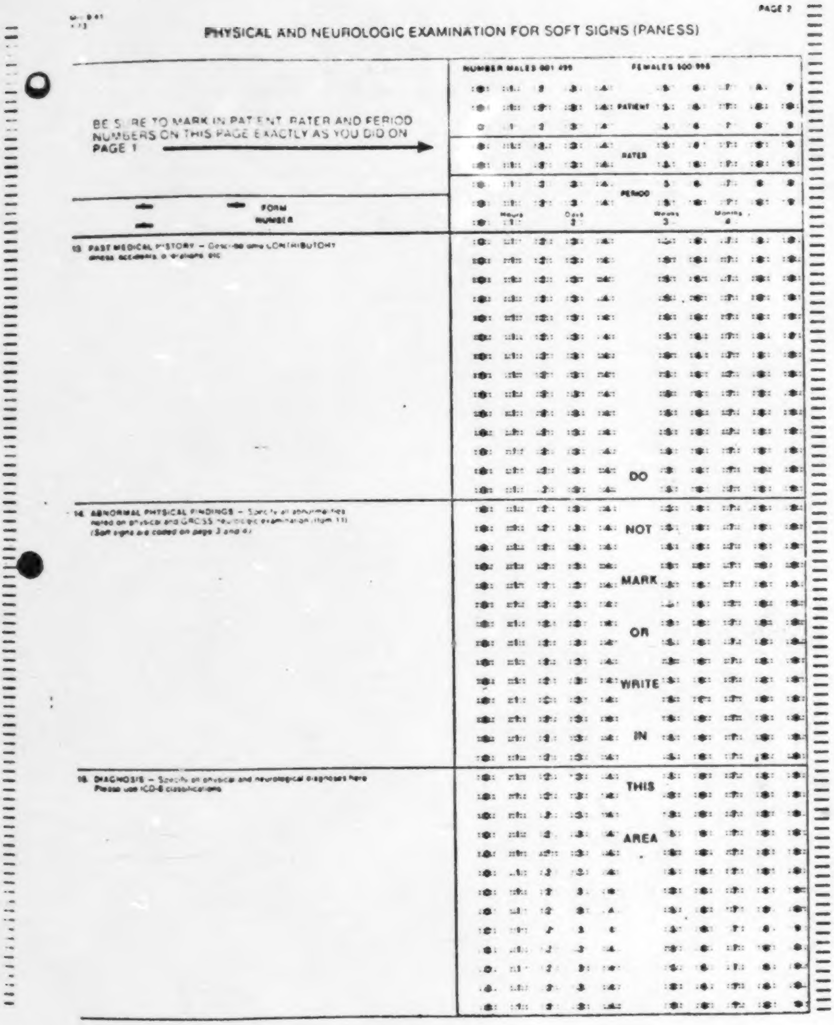
*Specify abnormalities under item 14

11. PHYSICAL EXAMINATION – Specify any abnormal findings under item 14

	Normal	Abnormal	NA
A HEENT	0	1	2
B NECK	0	1	2
C CARDIOVASCULAR	0	1	2
D PULMONARY	0	1	2
E LIVER	0	1	2
F KIDNEY	0	1	2
G SPLEEN	0	1	2
H OTHER ABDOMINAL	0	1	2
I MUSCULOSKELETAL	0	1	2
J GROSS NEUROLOGIC	0	1	2
K SKIN	0	1	2
L LYMPHATICS	0	1	2
M G U	0	1	2

12. Was the neurological examination for soft signs conducted and coded on pages 3 and 4 of this form?

NO 0 YES 1



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PAGE 2

PHYSICAL AND NEUROLOGIC EXAMINATION FOR SOFT SIGNS (PANESS)

BE SURE TO MARK IN PATIENT, RATER AND PERIOD NUMBERS ON THIS PAGE EXACTLY AS YOU DID ON PAGE 1

NUMBER MALES 001-499 FEMALES 500-998

PATIENT

RATER

PERIOD

Hours 1

Days 2

Weeks 3

Months 4

FORM NUMBER

13. PAST MEDICAL HISTORY – Describe any CONTRIBUTORY illness, accidents, operations, etc.

14. ABNORMAL PHYSICAL FINDINGS – Specify all abnormalities noted on physical and GROSS neurologic examination (Item 11) (Soft signs are coded on page 3 and 4)

15. DIAGNOSIS – Specify all physical and neurological diagnoses here. Please use ICD-8 classifications

DO NOT MARK OR WRITE IN THIS AREA

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PAGE 3

PHYSICAL AND NEUROLOGIC EXAMINATION FOR SOFT SIGNS (PANESS)

BE SURE TO MARK IN PATIENT, RATER AND PERIOD NUMBERS ON THIS PAGE EXACTLY AS YOU DID ON PAGE 1 →

NUMBER MALES 001-499 FEMALES 500-999

	0	1	2	3	4		5	6	7	8	9
PATIENT	0	1	2	3	4		5	6	7	8	9
	0	1	2	3	4		5	6	7	8	9
RATER	0	1	2	3	4		5	6	7	8	9
	0	1	2	3	4		5	6	7	8	9
PERIOD	0	1	2	3	4		5	6	7	8	9
	0	1	2	3	4		5	6	7	8	9
	0	Hours 1		Days 2			Weeks 3		Months 4		

DATE FORM NUMBER

USE THIS CODE FOR ITEMS 1-20 * SEE INSTRUCTIONS IN ASSESSMENT MANUAL FOR DETAILS

1 — Performed correctly
2 — Performed but not well
3 — Performed poorly or only after repeated instruction and demonstration
4 — Unsuccessful even after repeated demonstration
9 — Not done or not ascertained

1. Touch your finger to your nose	1	2	3	4	9
2. Touch your other finger to your nose	1	2	3	4	9
3. Close your eyes and touch your finger to your nose	1	2	3	4	9
4. Close your eyes and touch your other finger to your nose	1	2	3	4	9
5. Touch one heel to your other leg	1	2	3	4	9
6. Do the same with your other heel	1	2	3	4	9
7. Close your eyes and do it again	1	2	3	4	9
8. Now the other heel	1	2	3	4	9

Child writes name at the top of separate sheet of paper. Trace a "8" in each palm and identify it for the child. Figure is drawn in palm as child would see it. "Close your eyes and I will draw a mark on your hand. Now open your eyes and draw it on paper."

9.	☐	Right Hand	1	2	3	4	9
10.	X	Left Hand	1	2	3	4	9
11.	O	Right Hand	1	2	3	4	9
12.	⊏	Left Hand	1	2	3	4	9
13.	X	Right Hand	1	2	3	4	9
14.	3	Left Hand	1	2	3	4	9
15.	O	Right Hand	1	2	3	4	9
16.	3	Left Hand	1	2	3	4	9

"Close your eyes and tell me what I'm putting in your hand."

17.	Coin	Right Hand	1	2	3	4	9
18.	Ring	Left Hand	1	2	3	4	9
19.	Safety Pin	Right Hand	1	2	3	4	9
20.	Key	Left Hand	1	2	3	4	9

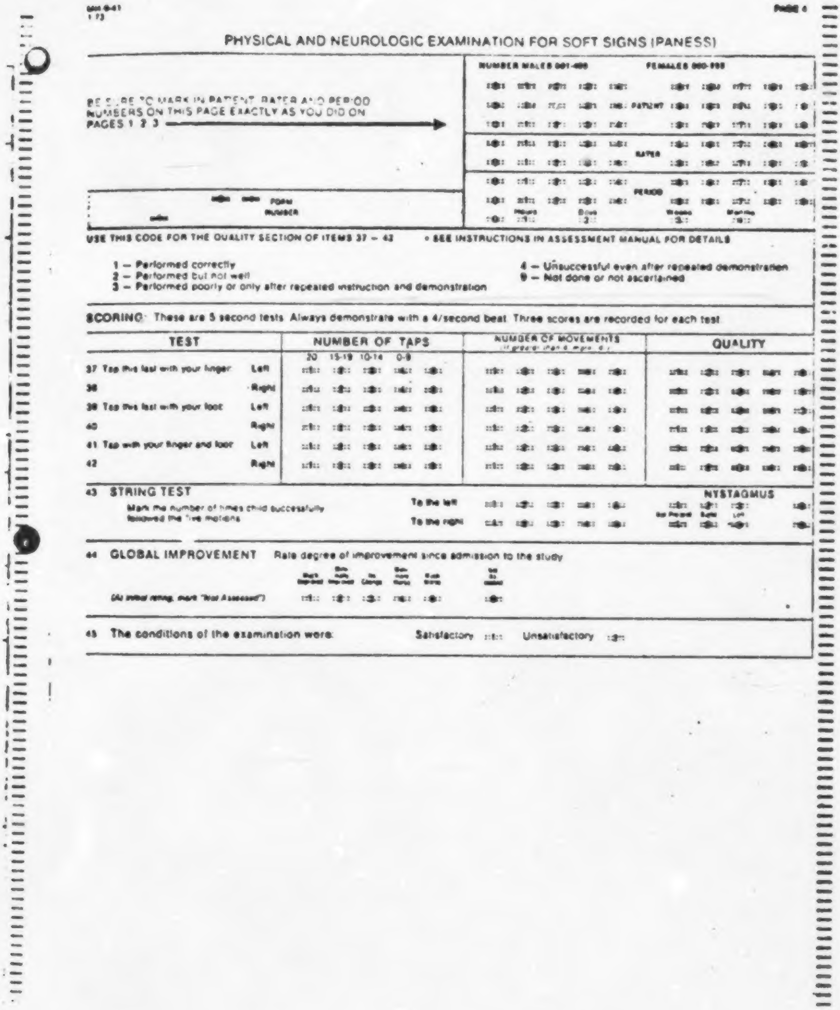
SCORING: Count number of errors (more than 3 scored as three). An error is definite deviation from the line or steps incorrectly done.

21. Walk the line to the end on your toes	0	1	2	3	9
22. Walk back on your heels	0	1	2	3	9
23. Hop on one foot to the end of the line	0	1	2	3	9
24. Now hop back on the other foot	0	1	2	3	9
25. Walk to the end this way (show tandem)	0	1	2	3	9
26. Now walk backwards the same way (6 steps)	0	1	2	3	9
27. FACE—HAND Brush face and/or hand gently with equal stroke (patient's eyes closed)	0	1	2	3	9
28. FACE—NOISE Brush face and/or click toy cricket ipsilateral ear (patient's eyes closed)	0	1	2	3	9
29. Two point discrimination, 1 cm. separation, dorsum of digiti minimi	0	1	2	3	9

PERSISTENCE MEASUREMENTS — Period of uninterrupted success (stopwatch)

	SECONDS				
	20	15-19	10-14	0-9	
30. Stick out your tongue until I tell you to stop	1	2	3	4	9
31. Raise your arms out in front of you until I tell you to stop	1	2	3	4	9
32. Close your eyes until I tell you to open them	1	2	3	4	9
33. Stand on one foot until I tell you to stop	1	2	3	4	9
34. Now stand on the other	1	2	3	4	9

	SECONDS				
	20	15-19	10-14	0-9	
35. Close your eyes and stand still until I tell you to stop	1	2	3	4	9
Tendency to fall?		NO 0		YES 1	9
36. Now do it again like this (Demonstrate tandem)	1	2	3	4	9
Tendency to fall?		NO 0		YES 1	9



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PAGE 4

PHYSICAL AND NEUROLOGIC EXAMINATION FOR SOFT SIGNS (PANESS)

BE SURE TO MARK IN PATIENT, RATER AND PERIOD NUMBERS ON THIS PAGE EXACTLY AS YOU DID ON PAGES 1 2 3 →

NUMBER MALES 001-499 FEMALES 500-999

PATIENT

RATER

PERIOD

FORM NUMBER

USE THIS CODE FOR THE QUALITY SECTION OF ITEMS 37 – 42 • SEE INSTRUCTIONS IN ASSESSMENT MANUAL FOR DETAILS

1 – Performed correctly
2 – Performed but not well
3 – Performed poorly or only after repeated instruction and demonstration
4 – Unsuccessful even after repeated demonstration
9 – Not done or not ascertained

SCORING: These are 5 second tests. Always demonstrate with a 4/second beat. Three scores are recorded for each test.

TEST		NUMBER OF TAPS	NUMBER OF MOVEMENTS	QUALITY
		20 15-19 10-14 0-9		
37 Tap this fast with your finger	Left	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○
38	Right	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○
39 Tap this fast with your foot	Left	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○
40	Right	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○
41 Tap with your finger and foot	Left	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○
42	Right	○ ○ ○ ○ ○	○ ○ ○ ○ ○	○ ○ ○ ○ ○

43 **STRING TEST**

Mark the number of times child successfully followed the five motions

To the left ○ ○ ○ ○ ○

To the right ○ ○ ○ ○ ○

NYSTAGMUS

44 **GLOBAL IMPROVEMENT** Rate degree of improvement since admission to the study

(At initial rating, mark "Not Assessed") ○ ○ ○ ○ ○ ○

45 The conditions of the examination were: Satisfactory ○ Unsatisfactory ○

QUESTIONNAIRE FOR CHILDREN WITH HYPERKINESIS OR LEARNING DIFFICULTY

(H-LD)

Child's Name ______________________________

I. Feeding in Infancy

Item

1. Anorexia — 1.____
   - no=0
   - yes=1
2. Breast Feed — 2.____
   - no=0
   - yes=1
   - If yes, how long?__________
3. Artificial Feeding — 3.____
   - no=0
   - yes=1
   - If yes, adverse reaction? — 4.____
     - no=0
     - yes=1
   - If yes, what type:
     - spitting?_____
     - vomiting?_____
     - flatulence (stomach or intestine gas)?_____
     - diarrhea?_____
     - constipation?_____
     - colic?_____
       - If colic, how long?____________
   - Type of formulae______________________
   - Frequently changed?________________
4. Addition of solid foods--what age?___________
   - Type of solid food: — 5.____
     - cereal=1
     - meat=2
     - vegetables=3
     - fruit=4
     - fruit juices=5
5. Vitamins--type and dose ______________________________

II. Review of Systems

6. Facial expression
   - pallor — 6.____
     - no=0
     - yes=1
   - dark circles beneath eyes — 7.____
     - no=0
     - yes=1
   - mouth breather — 8.____
     - no=0
     - yes=1

dental malocclusion 9.____
no=0
yes=1

7. Head
cradle cap 10.____
no=0
yes=1
If yes, how long?____________

8. Eyes
itching 11.____
no=0
yes=1
burning 12.____
no=0
yes=1
swelling 13.____
no=0
yes=1
redness 14.____
no=0
yes=1
blepharitis (i.e., redness, thickening
or scaling of lid margins) 15.____
no=0
yes=1
visual acutiy 16.____
no=0
yes=1

9. Ears
serous otitis (fluid in the ear) 17.____
no=0
yes=1
If yes, number of episodes__________
date of last episode______________
treatment--tubal drainage, etc.______________
purulent otis (pus in middle ear) 18.____
no=0
yes=1
If yes, number of episodes__________
date of last episode__________
treatment____________________
hearing acuity, problem 19.____
no=0
yes=1
If yes, specific nature__________________

10. Nose
snifflles in infancy 20.____
no=0
yes=1
If yes, until what age?____________
past infancy:
sneezing--paroxysms 21.____
no=0
yes=1

rhinorrhea (running nose) 22.____
no=0
yes=1
stopped nose 23.____
no=0
yes=1
itching 24.____
no=0
yes=1
If yes, does the child rub the nose with an upward motion of the back of the hand?__________
If yes, does the child have a crease above the tip of the nose?________
picking the nose 25.____
no=0
yes=1
nosebleeds 26.____
no=0
yes=1
nasal symptoms 27.____
no=0
yes=1
If yes, perennial?____________
perennial with seasonal exacerbations?_______
If yes, specify season___________

11. Throat
history of throat infection 28.____
no=0
yes=1
If yes, at what age did this occur?________
treatment?____________________
tonsillar involvement
T&A (tonsillectomy--adenoidectomy) 29.____
no=0
yes=1
If yes, when?__________
indication for T&A______________
response following T&A______________
itching of the palate 30.____
no=0
yes=1
history of croup 31.____
no=0
yes=1
If yes, at what age?___________

12. Lower Respiratory System
cough 32.____
no=0
yes=1
If yes, frequency____________________
season of year________________
dry or productive______________
nocturnal__________________
diurnal__________________

wheezing 33.____
no=0
yes=1
If yes, at rest?______________________
following laughing?______________
" crying?______________
" exertion?______________
dyspnea or exertion 34.____
no=0
yes=1
history of frequent bronchial (or chest) involvement 35.____
no=0
yes=1
If yes, in infancy?_________________
later childhood?______________
history of pneumonia 36.____
no=0
yes=1
If yes, X-Ray findings________________

13. Gastrointestinal (beyond infancy)
food intolerance 37.____
no=0
yes=1
If yes, milk?____________
any other food?______________

nature of intolerance:
vomiting?__________
cramps?__________
diarrhea?__________
constipation?__________
skin eruption?________
hives?________
swelling (angio-edema)?__________
stopped nose?______________
asthma or bronchitis?______________

14. Genito-urinary
eneuresis 38.____
no=0
yes=1
If yes, at what age?______________
duration_________________ __

15. Skin
cradle cap in infancy 39.____
no=0
yes=1
skin eruption 40.____
no=0
yes=1
If yes, at what age?_____ ______
distribution on the body:
bends of arms and legs?__________
elsewhere? (indicate) ____________________

character of skin eruption:
weeping?______________
dry?_________________
scaly?________________
thickened?______________
itching?_______________
duration of skin eruption______________________

related to ingestion of any food or beverage?________
environmental factor in home?___________________
to animals?__________________________

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CHILDREN'S DIAGNOSTIC CLASSIFICATION

INSTRUCTIONS *ONE RESPONSE and only ONE is permitted. Mark that response on ROW 31 in the column specified. Mark on General Scoring Sheet numbered 03.*

Rate current status only. Follow the items until you reach the most appropriate classification for the child.
Mark that response and *STOP*
Complete at pretreatment only

Proceed through sequence of YES–NO choice points and choose ONE. Mark that response in specified RESPONSE POSITION

1. Is significant psychopathology present?

YES – Go to 2
NO – Diagnose as NORMAL . . . . Mark and STOP 0

2. Is delirium present?

YES – Diagnose as ACUTE BRAIN SYNDROME . . . . Mark and STOP 1
NO – Go to 3

3. Is autism and/or thought disorder present?

YES – Diagnose as SCHIZOPHRENIA CHILDHOOD TYPE Mark and STOP 2
NO – Go to 4

4. Is subjective distress (anxiety, worries, etc.) expressed?

YES – Diagnose as OVERANXIOUS REACTION . . . . Mark and STOP 3
NO – Go to 5

5. Is there deliberate anti-social behavior and/or hostile conflict with environment (not simply explosive reaction to frustration)?

YES – Diagnose as UNSOCIALIZED AGGRESSIVE REACTION . . . . Mark and STOP 4
NO – Go to 6

6. Is antisocial behavior predominantly in peer group (gang) situation?

YES Diagnose as DYSSOCIAL REACTION . . . . Mark and STOP 5
NO – Go to 7

7. Is hyperactivity/attention disorder present?

YES – Diagnose as HYPERACTIVE REACTION . . . . . Mark and STOP 6
NO – Go to 8

8. Is shyness-withdrawal the *predominant* behavior pattern?

YES – Diagnose as WITHDRAWING REACTION . . . . Mark 7
NO – Diagnose as UNDIAGNOSED . . . . Mark 8

L-4

MARK ON ROW 31 ONLY

COLUMNS:	0	1	2	3	4	5	6	7	8	9
1	0	1	2	3	4	5	6	7	8	9
2	0	1	2	3	4	5	6	7	8	9
3	0	1	2	3	4	5	6	7	8	9
4	0	1	2	3	4	5	6	7	8	9
5	0	1	2	3	4	5	6	7	8	9
6	0	1	2	3	4	5	6	7	8	9
7	0	1	2	3	4	5	6	7	8	9
8	0	1	2	3	4	5	6	7	8	9
9	0	1	2	3	4	5	6	7	8	9
10	0	1	2	3	4	5	6	7	8	9
11	0	1	2	3	4	5	6	7	8	9
12	0	1	2	3	4	5	6	7	8	9
13	0	1	2	3	4	5	6	7	8	9
14	0	1	2	3	4	5	6	7	8	9
15	0	1	2	3	4	5	6	7	8	9
16	0	1	2	3	4	5	6	7	8	9
17	0	1	2	3	4	5	6	7	8	9
18	0	1	2	3	4	5	6	7	8	9
19	0	1	2	3	4	5	6	7	8	9
20	0	1	2	3	4	5	6	7	8	9
21	0	1	2	3	4	5	6	7	8	9
22	0	1	2	3	4	5	6	7	8	9
23	0	1	2	3	4	5	6	7	8	9
24	0	1	2	3	4	5	6	7	8	9
25	0	1	2	3	4	5	6	7	8	9
26	0	1	2	3	4	5	6	7	8	9
27	0	1	2	3	4	5	6	7	8	9
28	0	1	2	3	4	5	6	7	8	9
29	0	1	2	3	4	5	6	7	8	9
30	0	1	2	3	4	5	6	7	8	9
31	0	1	2	3	4	5	6	7	8	9
32	0	1	2	3	4	5	6	7	8	9
33	0	1	2	3	4	5	6	7	8	9
34	0	1	2	3	4	5	6	7	8	9
35	0	1	2	3	4	5	6	7	8	9
36	0	1	2	3	4	5	6	7	8	9
37	0	1	2	3	4	5	6	7	8	9
38	0	1	2	3	4	5	6	7	8	9
39	0	1	2	3	4	5	6	7	8	9
40	0	1	2	3	4	5	6	7	8	9
41	0	1	2	3	4	5	6	7	8	9
cols	11	12	13	14	15	16	17	18	19	20

MH 9-20
1-73

CLINICAL GLOBAL IMPRESSIONS

INSTRUCTIONS: *Mark these items on General Scoring Sheet coded 01.*

Complete Item 1 – SEVERITY OF ILLNESS at the initial and subsequent assessments. Items 2 and 3 may be omitted at the initial assessment by marking 0 – "Not Assessed"

Mark on the left half of the scoring sheet on rows 38 – 41.

Row										
1	0	1	2	3	4	5	6	7	8	9
2	0	1	2	3	4	5	6	7	8	9
3	0	1	2	3	4	5	6	7	8	9
4	0	1	2	3	4	5	6	7	8	9
5	0	1	2	3	4	5	6	7	8	9
6	0	1	2	3	4	5	6	7	8	9
7	0	1	2	3	4	5	6	7	8	9
8	0	1	2	3	4	5	6	7	8	9
9	0	1	2	3	4	5	6	7	8	9
10	0	1	2	3	4	5	6	7	8	9
11	0	1	2	3	4	5	6	7	8	9
12	0	1	2	3	4	5	6	7	8	9
13	0	1	2	3	4	5	6	7	8	9
14	0	1	2	3	4	5	6	7	8	9
15	0	1	2	3	4	5	6	7	8	9
16	0	1	2	3	4	5	6	7	8	9
17	0	1	2	3	4	5	6	7	8	9
18	0	1	2	3	4	5	6	7	8	9
19	0	1	2	3	4	5	6	7	8	9
20	0	1	2	3	4	5	6	7	8	9
21	0	1	2	3	4	5	6	7	8	9
22	0	1	2	3	4	5	6	7	8	9
23	0	1	2	3	4	5	6	7	8	9
24	0	1	2	3	4	5	6	7	8	9
25	0	1	2	3	4	5	6	7	8	9
26	0	1	2	3	4	5	6	7	8	9
27	0	1	2	3	4	5	6	7	8	9
28	0	1	2	3	4	5	6	7	8	9
29	0	1	2	3	4	5	6	7	8	9
30	0	1	2	3	4	5	6	7	8	9
31	0	1	2	3	4	5	6	7	8	9
32	0	1	2	3	4	5	6	7	8	9
33	0	1	2	3	4	5	6	7	8	9
34	0	1	2	3	4	5	6	7	8	9
35	0	1	2	3	4	5	6	7	8	9
36	0	1	2	3	4	5	6	7	8	9
37	0	1	2	3	4	5	6	7	8	9
38	0	1	2	3	4	5	6	7	8	9
39	0	1	2	3	4	5	6	7	8	9
40	0	1	2	3	4	5	6	7	8	9
41	0	1	2	3	4	5	6	7	8	9
Col.	1	2	3	4	5	6	7	8	9	10

CLINICAL GOBAL IMPRESSIONS

ROW NO.

38 1. **SEVERITY OF ILLNESS**

Considering your total clinical experience with this particular population, how mentally ill is the patient at this time?

0 = Not assessed	4 = Moderately ill
1 = Normal, not at all ill	5 = Markedly ill
2 = Borderline mentally ill	6 = Severely ill
3 = Mildly ill	7 = Among the most extremely ill patients

THE NEXT TWO ITEMS MAY BE OMITTED AT THE INITIAL ASSESSMENT BY MARKING "NOT ASSESSED" FOR BOTH ITEMS

39 2. **GLOBAL IMPROVEMENT** – Rate total improvement whether or not in your judgment, it is due entirely to drug treatment.

Compared to his condition at admission to the project, how much has he changed?

0 = Not assessed	4 = No change
1 = Very much improved	5 = Minimally worse
2 = Much improved	6 = Much worse
3 = Minimally improved	7 = Very much worse

40 & 41 3. **EFFICACY INDEX** – Rate this item on the basis of DRUG EFFECT ONLY.

Select the terms which best describe the degrees of therapeutic effect and side effects and record the number in the box where the two items intersect.

EXAMPLE: Therapeutic effect is rated as "Moderate" and side effects are judged "Do not significantly interfere with patient's functioning". Record 06 in rows 40 and 41.

THERAPEUTIC EFFECT	SIDE EFFECTS			
	None	Do not significantly interfere with patient's functioning	Significantly interferes with patient's functioning	Outweighs therapeutic effect
MARKED – Vast improvement. Complete or nearly complete remission of all symptoms	01	02	03	04
MODERATE – Decided improvement. Partial remission of symptoms	05	06	07	08
MINIMAL – Slight improvement which doesn't alter status of care of patient	09	10	11	12
UNCHANGED OR WORSE	13	14	15	16
Not Assessed = 00				

R-3 R-3

CGI

[illegible]
1-73

CHILDREN'S DIAGNOSTIC SCALE

INSTRUCTIONS *Insert New General Scoring Sheet and Code 03 under Sheet Number.*

Responses should be based on overall psychiatric judgments utilizing all data sources integratively, e.g., school reports, mother's reports, interview data, etc.

Rate current status only. Be sure to answer all items.

Complete at pretreatment only.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE YOUR MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

NOT ASSESSED	NOT PRESENT	VERY MILD	MILD	MODERATE	MODERATELY SEVERE	SEVERE	EXTREMELY SEVERE

Mark each item on right half of scoring sheet on row specified

			ROW NO.
1.	**PSYCHOTICISM** Gross impairment of relationships with people and environment, bizarre interaction, extreme preoccupation with internal stimuli, responses appear markedly inappropriate to external stimuli and/or displays distinct thinking disorders, neologisms, echolalia, incoherence, confused, irrelevant or tangential content, or confused about reality or mistrust or bizarre ideation, delusions, hallucinations, or permeated by [illegible] of illustrations, illogical or contradictory statements.		1
2.	**ANXIETY REACTION** *Expresses* feelings of nervousness, anxiety, unrealistic fears or worries, concern with feelings of inadequacy, inferiority, shyness, obsessions or compulsions.		2
3.	**WITHDRAWAL REACTION** Isolation, seclusiveness, withdrawal, detachment, inability to form close relationships.		3
4.	**UNSOCIALIZED AGGRESSIVE BEHAVIOR** Overtly negative, defiant, hostile, and/or manipulative, evasive, guarded. Attempts to control others, aggressive, antisocial, overwhelmingly selfish. Denial of anxiety and personal responsibility for feelings and acts. Is in hostile conflict with the environment in a variety of social settings (family, school) which do not involve group expression of hostility.		4
5.	**SOCIALIZED AGGRESSIVE BEHAVIOR** Is in delinquent or hostile conflict with the environment, primarily in association with members of a gang, rarely on own.		5
6.	**EXPLOSIVE AGGRESSION** Unable to control appropriately his responses towards peers and/or adults. Physically aggressive, impulsive, often reacts to others before understanding the meaning or motives of their words or actions. Gets into numerous fights. Physically disruptive particularly in classroom where he may hit out at others with little or no provocation.		6
7.	**CHRONIC HYPERACTIVITY** High and continuous level of gross motor activity in a variety of settings such as school, home, stores, office, etc.		7
8.	**IMMATURE AND INADEQUATE BEHAVIOR** Variable and poorly organized personality characteristics and coping techniques.		8
9.	**PRESENCE OF GROSS ORGANIC IMPAIRMENT** Do not include impression of minimal brain damage, but use all available examinational data such as neurological tests, EEG, etc. Gross organic impairment refers to findings which lead to a strong inference of anatomical lesions or organic diagnoses, e.g., hemiparesis, cerebral palsy, epilepsy, etc. If YES, specify PSYCHIATRIC diagnosis (DSM II) in item 12b and/or 12c. Any neurologic diagnosis without associated psychopathology should be specified on the Physical and Neurological Examination form, form number 41.	0 = NO 1 = YES	9
10.	**DELIRIUM** Gross acute impairment of orientation (time, place or person) and/or memory, with clouding of sensorium. Unlike item 9, delirium should imply reversible organic impairment. If YES, specify PSYCHIATRIC diagnosis (DSM II) in item 12b and/or 12c. Any neurologic diagnosis without associated psychopathology should be specified on the Physical and Neurological Examination form.	0 = NO 1 = YES	10
11.	**PRESENCE OF GROSS MENTAL RETARDATION** Obvious to the examiner and/or found on psychometric tests. If YES, specify diagnosis in item 12b and/or 12c.	0 = NO 1 = YES	11

L-6

Continue marking on right half of scoring sheet on specified row

			ROW NO.
12.	**DIAGNOSIS**		12
	(a)	Specify ONE of the following diagnoses on row 12 OR record any other DSM II diagnosis under (b) and/or (c) below. 1 - Schizophrenia, childhood (295.8) 2 - Overanxious reaction (308.2) 3 - Unsocialized aggressive reaction (308.4) 4 - Hyperactive reaction (308.0) 5 - Withdrawal reaction (308.1) 6 - Diagnosis cannot be formulated but significant psychopathology is present 7 - No significant psychopathology (318.0)	
	(b)	Other diagnosis # 1 . . . . Mark on 4 rows	13-16
	(c)	Other diagnosis # 2 . . . . Mark on 4 rows	17-20
13.	**SPECIAL SYMPTOMS** Check presence of a symptom by marking "5" on the proper row. If no special symptoms present mark "5" on row 21.		
	A.	No symptoms	21
	B.	Speech disturbance	22
	C.	Specific learning disturbance . .	23
	D.	Tic	24
	E.	Other psychomotor disorder . .	25
	F.	Disorder of sleep	26
	G.	Feeding disturbance	27
	H.	Enuresis	28
	I.	Encopresis	29
	J.	Cephalalgia	30

L-7

MH-9-27
1-73

CHILDREN'S PSYCHIATRIC RATING SCALE

C
P
R
S

INSTRUCTIONS. *Insert General Scoring Sheet, Form 60, and Code 01 under Sheet Number.*

Rate the first 28 items exclusively on the basis of direct observation during the interview.

Rate the last 34 items (29–63) on the basis of the child's verbal report of occurrence at the time of the interview or during the past seven days. Do not use any other data, but that obtained in the interview with the child.

Mark all rows consecutively – do not skip any rows. Each row is numbered on the scoring sheet and also on the page with the item to facilitate marking on the correct row.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE.

NOT SCORED · NOT PRESENT · VERY MILD · MILD · MODERATE · MODERATELY SEVERE · SEVERE · EXTREMELY SEVERE

Mark on right half of scoring sheet on row specified	ROW NO.
1. **TENSION** *(Do not include fidgetiness)* Musculature appears taut, strained or tense. Fingers clutching, clenches jaw, grips arms of chair, hands tremulous.	1
2. **UNDERPRODUCTIVE SPEECH** *(Rate amount of speech only, not rate or relevance)* Fails to answer questions, monosyllabic, has to be pushed to get an answer, answers delayed, blocking.	2
3. **FIDGETINESS** *(Do not include tics)* Wriggles, squirms, moves or shifts restlessly in chair.	3
4. **HYPERACTIVITY** Has difficulty sitting in chair, gets up, moves fast, vigorously, impulsive bursts of locomotion. Exclude slow ambling even if constant. In rating degree of overactivity, consider the ease with which the hyperactivity can be controlled.	4
5. **HYPOACTIVITY** Few or no spontaneous movements. Sluggish. Movements are slowed, feeble or labored. Requires prompting for initiation of motor movements. Long latencies of appropriate motor behavior.	5
6. **DISTRACTIBILITY** Distracted by usually minor, irrelevant stimuli. Shifts from one topic to another. Interrupts thought or act on [illegible].	6
7. **ABNORMAL OBJECT RELATIONSHIPS** Autistic use of objects with disregard for usual function. Stereotyped and repetitive sequences or fragments of play. Aimless behavior without organizing goal idea.	7
8. **WITHDRAWAL** Oblivious of examiner, preoccupied. Facial expression and behavior do not respond directly to examiner. Attention focus is [illegible] with avoidance of eye contact. [illegible] stimuli. *(The fact that the child may have peculiar interest in examiner, such as obsessive interest in parts of body or clothing does not preclude a rating of withdrawal.)*	8
9. **OVERCOMPLIANT** Goes along with whatever examiner says in a passive fashion, even contradicting self. Does not assert self in any [illegible] manner.	9
10. **NEGATIVE, UNCOOPERATIVE** Active opposition and resistance to examiner's invitation. *(Differs from withdrawn and aloof behavior.)* [illegible] to active refusal to cooperate. Child may remain silent in passive aggressive fashion.	10
11. **ANGRY AFFECT** Irritable, touchy, irascible, hostile, shouts angrily, screams at examiner, overtly and directly hostile.	11

L-1

Continue marking on right half of scoring sheet on row specified	ROW NO.
12. **SILLY AFFECT** Clowning, inappropriately giddy, playful, silly behavior.	12
13. **CONFUSION** Confused, bewildered, perplexed in behavior or verbal expression.	13
14. **DISORIENTATION** Child is unaware of identity of surroundings after being told where he is. Not aware of time discriminations. Doesn't know age or surname.	14
15. **CLINGING BEHAVIOR** Clinging in physical and verbal behavior with the examiner. Seeks physical contact, demands constant direction.	15
16. **UNSPONTANEOUS RELATION TO EXAMINER** Responds to examiner, but does not initiate social or verbal [illegible], not sustain conversation once begun. Lacks spontaneity. Restricted.	16
17. **SUSPICIOUS AFFECT** Expresses concern about the intent of the examination. Questions instructions and good will of interviewer.	17
18. **DEPRESSED DEMEANOR** Exhibits dejection, depression in mood. Looks sad. Seems to be in a state of painful dejection.	18
19. **BLUNTED AFFECT** Restricted range and intensity of emotional expressions. Blank or fixed facial expression, monotonous voice.	19
20. **LABILITY OF AFFECT** Can suddenly vary from calm or silly to sullen mood, to screaming, crying, loud complaining.	20
21. **PRESSURE OF SPEECH** Speech is hurried, accelerated, pushed, difficult to interrupt.	21
22. **LEVEL OF SPEECH DEVELOPMENT** *(Do not include diction, rate of speech, or relevance of speech)* From age-appropriate (1) to severely retarding (7) speech development. Using your clinical judgment of verbal I.Q., estimate the level of speech development (in percent) in relation to verbal I.Q. 1 = Over 90% 2 = 76 – 90% 3 = 61 – 75% 4 = 46 – 60% 5 = 31 – 45% 6 = 16 – 30% 7 = Less than 15%	22
23. **STUTTERING**	23
24. **LOW VOICE** Voice weak, mumbling, whispering, almost inaudible.	24
25. **LOUD VOICE** Voice loud, boisterous, shouting.	25

L-2

MH 9-39
1-73

CHILDREN'S PSYCHIATRIC RATING SCALE

C
P
R
S

INSTRUCTIONS: *Insert General Scoring Sheet, Form 50, and Card 01 under Sheet Number*

Rate the first 28 items exclusively on the basis of direct observation during the interview.

Rate the last 34 items (29–63) on the basis of the child's verbal report of occurrence at the time of the interview or during the past seven days. Do not use any other data, but that obtained in the interview with the child.

Mark all rows consecutively – do not skip any rows. Each row is numbered on the scoring sheet and also on the page with the item to facilitate marking on the correct row.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE

NOT TO BE SCORED | NOT PRESENT | VERY MILD | MILD | MODERATE | MODERATELY SEVERE | SEVERE | EXTREMELY SEVERE

Continue marking on right half of scoring sheet on row specified — ROW NO.

26. MISPRONUNCIATIONS — 26

Lisping, mispronounces letters such as r, s, l, etc. Unclear speech.

27. OTHER SPEECH DEVIANCE — 27

Echolalia, question-like melody, neologisms, sentences fragmented, unusual syntax.

28. RHYTHMIC MOTIONS (STEREOTYPE) — 28

Rocking, whirling, head banging, rolling, repetitive jumping, hand movements, whirling, twirling with fingers.

RATE THE FOLLOWING 34 ITEMS ON THE BASIS OF THE CHILD'S VERBAL REPORT OF OCCURRENCE AT THE TIME OF THE INTERVIEW OR DURING THE PAST 7 DAYS. DO NOT USE ANY OTHER DATA BUT THAT OBTAINED IN INTERVIEW WITH THE CHILD

29. EXPRESSED FEELINGS OF INFERIORITY — 29

Overt feelings of inadequacy, inferiority, self depreciating, self belittling.

30. EXPRESSED FEELINGS OF GRANDIOSITY — 30

Exaggerates own value, boasting. Unduly pleased with own achievement. Says he is much better than others. Distorted sense of own capacity.

31. PHYSICAL COMPLAINTS — 31

Somatic complaints of headaches, stomach aches, dizziness, not feeling well, etc. (do not include fatigue)

32. OBESITY — 32

Judge from child's appearance from normal physical appearance to severe obesity.

33. OTHER EATING PROBLEMS — 33

Picky, fussy, many dislikes, extremely restricted diet, peculiar food tastes.

34. SEPARATION ANXIETY — 34

Ease with which child separates from mother or other significant people. Extent of observed or reported anxiety (by child) experienced by child when separated from mother or other significant people.

35. DEPRESSION — 35

Admits feeling sad, lonely, feels like crying, expresses a despondent or discouraging attitude. Difficulty in anticipating success and enjoyment.

36. EUPHORIA – ELATION — 36

States he feels terrific, great, elevation of mood. Hypomanic state. "This is the best of all possible worlds." Feels elated and wonderful. Nothing is impossible.

37. LACK OF ENERGY — 37

States he feels sluggish, fatigued. Everything is too much. Weary and feels unable to muster slightest effort. (Do not infer from motor retardation or depressed and listless.)

L-3

NOT TO BE SCORED | NOT PRESENT | VERY MILD | MILD | MODERATE | MODERATELY SEVERE | SEVERE | EXTREMELY SEVERE — ROW NO.

When you have completed this page (item 41), turn all pages on this side and continue with text (item 42) on page R1

38. PREOCCUPATION WITH TOPICS OF ANXIETY — 38

Says he has nervous or scary feelings, concerns, apprehension, fears. Says he worries about failure or other mishaps, thinks about something happening to self or parents: illness, injury, death, loss or separation.

39. PREOCCUPATION WITH DEPRESSIVE TOPICS — 39

Preoccupied with feelings of inadequacy and inferiority. Expresses feeling that nothing can turn out all right. Preoccupied with feelings of unhappiness, loneliness, and possibly guilt. Suicidal preoccupation.

40. SUICIDAL ATTEMPTS — 40

0 = Not assessed
1 = None
2 = Suicidal threat
3 = One minor gesture without danger
4 = A couple or several minor gestures without danger
5 = Dangerous gesture
6 = Infliction of life threatening damage to self
7 = Several life threatening attempts

41. FEARS AND PHOBIAS — 41

Intense and morbid fears of specific objects, persons, or situations, which, if extreme, lead to avoidance behavior. Rate 6 or 7 only when fear is so severe it leads to phobic avoidance.

Turn all pages on this side and continue with item 42 on R-1

L-4

MH 9-37
1-73

CHILDREN'S PSYCHIATRIC RATING SCALE

CPRS

INSTRUCTIONS: *Insert General Scoring Sheet, Form 50, and Code 01 under Sheet Number.*

Rate the first 28 items exclusively on the basis of direct observation during the interview.

Rate the last 34 items (29 - 63) on the basis of the child's verbal report of occurrence at the time of the interview or during the past seven days. Do not use any other data, but that obtained in the interview with the child.

Mark all rows consecutively – do not skip any rows. Each row is numbered on the scoring sheet and also on the page with the item to facilitate marking on the correct row.

USE A NO. 2 LEAD PENCIL. BE SURE TO MAKE MARKS HEAVY AND DARK. ERASE COMPLETELY ANY MARKS YOU WISH TO CHANGE

NOT ASCERTAINED | NOT PRESENT | VERY MILD | MILD | MODERATE | MODERATELY SEVERE | SEVERE | EXTREMELY SEVERE

ROW NO.		*Mark on left half of scoring sheet on row specified*
1	42.	**COMPULSIVE ACTS** Acts or "habits" which are regarded as unreasonable by the child such as counting, checking, rituals, excessive orderliness, and cleanliness.
2	43.	**NERVOUS HABITS AND MANNERISMS** Stereotyped movements, rituals which are not perceived as irrational. Facial tics or mannerisms. Biting of nails, fingers, cuticles. Sucking of or on other body parts (thumb, fingers, hair, etc.). Picking on skin, scabs, nose; twisting hair.
3	44.	**OBSESSIVE THINKING** Inability to "turn off" repetitive thought. Preoccupation, ruminations about abstract problems or personal matters.
4	45.	**SOLITARY INTERESTS** Interested in activities which require little if any peer interaction, such as stamp collecting, movie going, reading, school work, solitary activities.
5	46.	**LACK OF PEER INTERACTION** Isolated from other children. Has no friends or cannot name current close friend nor describe participation in play with peers. Lacks interest in peers.
6	47.	**GANG ACTIVITY** Joins in antisocial activities along with a group of children (fighting, trouble making, stealing) as a cooperating group against others.
7	48.	**FIGHTING WITH PEERS** Says he frequently gets into fights – beats up other kids or gets beaten up. Says he has a bad temper.
8	49.	**BULLY** Says he's always the leader, winner, or says he teases, bullies children, pushes children around, threatens them.
9	50.	**TEMPER OUTBURSTS** Admits to feeling angry, irritable, touchy; admits he has a temper.
10	51.	**SCAPEGOAT** Says he's picked on, teased, left out or pushed around, and bullied by other children. May be called "sissy" or "baby".
11	52.	**LYING** Contradicts self in overt indication of effort to hide the truth. Reports telling tall stories, fibs, or admits he's accused of telling lies.
12	53.	**EXPLOITATIVE RELATIONSHIPS** Interested in other people insofar as he can get something out of it. Callous and calculating in interpersonal activities.

R-1

CPRS

NOT ASCERTAINED | NOT PRESENT | VERY MILD | MILD | MODERATE | MODERATELY SEVERE | SEVERE | EXTREMELY SEVERE

ROW NO.		*Continue marking on left half of scoring sheet on row specified*
13	54.	**INABILITY TO FALL ASLEEP** Child reports a long time to fall asleep after going to bed. 1 = Not present 2 = 10 to 15 min. 3 = 16 to 30 min. 4 = 31 to 45 min. 5 = 46 to 60 min. 6 = 60 to 90 min. 7 = Over 90 min.
14	55.	**OTHER SLEEP DIFFICULTIES** Nightmares, early morning awakening, sleep walking, interrupted sleep.
15	56.	**BEDWETTING** Rating is for frequency of bedwetting for past 7 nights. 1 = None 2 = One time 3 = 2 times 4 = 3 times 5 = 4 times 6 = 5 times 7 = 6 to 7 times
16	57.	**IDEAS OF REFERENCE** People are talking about him, laughing at him, watching, etc. Malevolent intent is not necessary but may occur.
17	58.	**PERSECUTORY** Feels people have it in for him, try to hurt him. In the extreme rating, the thinking has a delusional quality in that the belief is impervious to change (rational arguments, or corrective experiences).
18	59.	**OTHER THINKING DISORDERS** Irrelevant speech, or incoherent speech, or loose associations.
19	60.	**DELUSIONS** Delusional beliefs or convictions besides paranoia (58), i.e., believes has unexpected persons or objects in his body, has a mission, is some other person or character, has unusual powers, is guilty of some event.
20	61.	**HALLUCINATIONS** The overall rating is a frequency rating reflecting the constancy of the experience. 1 = Not present 2 = Once 3 = 2 times 4 = 3 times 5 = 4 to 5 times 6 = 5 to 8 times 7 = Daily recurrent phenomenon
21	62.	**PECULIAR FANTASIES** Morbid or bizarre fantasies and preoccupations, peculiar body sensations, distortions of body image experiences (incl. figure drawings), preoccupation with flying, supernatural influences, sadism, masochism.
22	63.	**LACK OF INSIGHT** Is convinced of the reality of hallucinations or fantasies.

R-2

END – CPRS

D. HYPERACTIVE REACTION (308.0)

NECESSARY & SUFFICIENT SYMPTOMS

Hyperactivity - with a high and conspicuous level of gross motor activity (locomotion; or "rump" hyperactivity when seated, i.e., squirming, changing position and getting up and down frequently; but not finger-hand-twisting, picking or other small muscle activity) occurring across environments in situations in which sedentary or quiet behavior is appropriate for age.

and

Disorder of attention - with higher distractability and shorter attention span than appropriate for chronological age (not mental age) especially in school, or group situations.

SYMPTOMS COMMONLY ASSOCIATED BUT NOT SUFFICIENT FOR DIAGNOSIS

Poorly integrated and labile behavior, which gives the impression of immaturity and of uneven but generally inadequate abilities.

Extremely variable relation to adults (including examiner), with rapid fluctuation from attempts at compliance to silly clowning, boisterous, mischievous or impertinent behavior, clinging and demanding behavior and/or angry or sullen negativism.

Labile affect. React with excessive irritability to any situation interpreted as rejecting demanding or restricting, with angry, suspicious, anxious, unhappy and silly clowning responses, often associated with gross motor discharge, tantrums, destructive or aggressive behavior.

Speech is often sparse and unelaborated with a tendency to evade emotionally charged material.

Fantasy is usually expressed more clearly in play; concerned with movement and aggression, diffuse fears of retaliation and loss of love.

Motility usually variable, impulsive and poorly coordinated. Movements are relatively undifferentiated for age; have difficulty suppressing gross body movement when attempting isolated, finely coordinated finger - hand or arm movements. Body manipulation relatively uninhibited for age; chewing, sucking, nose picking, masturbation.

Unable to conform to demands of a group situation with peers; often become scapegoats and/or participate peripherally by provocative, silly, teasing, aggressive, quarrelsome behavior; usually considered "babies" and "pests" by peers.

Adults usually consider them immature, demanding, difficult to manage. Have chronic and recurring difficulties in adapting to age-appropriate social and educational demands.

DISQUALIFIERS

Psychosis - If so permeated by autistic preoccupations or thought disorder, as defined under schizophrenia, as to necessitate a diagnosis of psychosis, then classify as Childhood Schizophrenia. Expressed preoccupation with anxiety and sadness which is pervasive, NOT transient.

Unsocialized Aggressive Reaction with organized behavior pattern. See discussion under "Unsocialized Aggressive Reaction", "Disqualifiers".

Diet Diary Procedures

Thank you for helping in this test of two diets.

Attached is a diet diary form which must be filled out for ______________ days during the ____ _________ week of the diet trial period. Please keep the record for ___________ _________________________________.

Everything the child eats and drinks needs to be recorded.

1. Record the time of day for meals and snacks.
2. Record the place where the food was eaten (home, school, restaurant, outside house).
3. Record what the food or beverage is (milk, hamburger, bun) include the brand name if known.
4. Record the description or method of preparation (milk - whole, hamburger - broiled with butter). If the food is a casserole or mixture, list the main ingredients (macaroni and cheese - enriched macaroni, Cheddar cheese, whole milk).
5. Record the amount of the food eaten by weight or common househood measure (3 ounces, 2/3 cup, 1 tablespoon).

At the end of each day or after each meal, record all the child has eaten, asking him about foods he ate away from home and using your combined memories for what he ate while at home and at school. Write it down by meal and snacks. Also record how well you feel he followed the diet and other comments (child sick, child followed diet easily).

At the end of the three days, please mail the records in the preaddressed envelope provided. Please call us if you have any questions or problems.

Instructions for Management with the H Diet (K-P Diet)

1. The diet lists all foods and products that are to be prohibited.

2. Any item not on the list is permitted. It is necessary to check every food package or container very carefully for artificial colors and flavors. In many cases, specific flavor or color is not indicated - avoid foods labeled with artificial or imitation flavors and artificial or U.S. certified colors. When in doubt, do not experiment - eliminate the food item.

3. With the difficulty in obtaining many food items on the market that conform to the allowed food list, it will be necessary to prepare many foods at home. Examples of this would be main dishes, candy, soups, puddings, and cakes. All beverages must be checked very carefully.

4. The greatest success is usually observed when the entire family follows the diet. This removes the temptations from the child and facilitates compliance with the diet.

5. It is important that the child and family continue maintaining adequate nutrition during the study. For this reason, the foods on the allowed list have been grouped according to their contribution to the diet. A balanced diet which will maintain the nutritional status of the individuals following the diet can be achieved by choosing a certain number of foods from each group, to be eaten each day. The minimum number of servings from each group is suggested as follows:

Child	Adult
4 cereal and grains	4 cereal and grains
2 fruits (1 good source of vitamin C)	2 fruits (1 good source of vitamin C)
2 vegetables	2 vegetables
2 protein sources	2 protein sources
2-3 dairy products also supplies protein	2 dairy products - also supplies protein

The foods listed under miscellaneous and beverages may be used as desired to complete the daily diet. This grouping of foods allows the child and family to choose a variety of food items which they like and will insure sound nutrition.

6. It is important to keep a diet diary for the days specified. This is the only method of control, as inadvertant infractions can be detected, and allows us to monitor your intake for nutrient adequacy.

7. You are asked to keep a daily record of infractions. We would hope that none occur. However, should infractions occur, it is important that you list all of them.

Diet H

These foods are to be ELIMINATED from diet

Cereals and Grain Products
All breakfast cereals with artificial colors or flavors
All cakes, cookies, pastries, sweet rolls, donuts, breads, etc., with artificial flavors or colors (i.e., from bakery)
Manufactured pie crusts
Frozen baked mixes
Prepared poultry stuffing

Fruits
Almonds
Apples
Apricots
Berries - blackberries, blueberries, boysenberries, gooseberries, raspberries, strawberries
Cherries
Currants - grapes and raisons or any products made of grapes, (e.g., wine, wine vinegar, jellies, etc.)
Nectarines
Oranges
Peaches

Vegetables
Tomatoes and all tomato products
Cucumbers (pickles)

Protein Sources
Meats
  Bologna, luncheon meats*
  Salami
  Frankfurters
  Sausage*
  Meat loaf*
  Ham, bacon, pork*
  All barbecued types of chicken
  All turkey prepared with basting, called "self-basting"
  Frozen fish fillets that are dyed or flavored - fish sticks or patties, typed or flavored

*When flavored or colored (usually indicated on package)

Dairy Products
Manufactured ice cream or ice milk unless label specifies no snythetic coloring or flavoring
Colored cheeses (i.e., processed or yellow (orange)
All instant breakfast drinks and preparations
Flavored yogurt
Prepared chocolate milk
Colored butter

DIET E

PERMITTED food items

Cereal and Grain Products
Any cereal without artificial colors or flavors, dry or cooked
Any baked goods without artificial color or flavor - most baked goods will have to be prepared at home
All flours
All commercial breads except egg brand (usually dyed)

Fruits
Grapefruit*
Lemon*
Lime*
Pear
Pineapple
Banana
Juices of these fruits* without artificial flavor or color

*Good sources of vitamin C, juices may be labeled "vitamin C enriched"

Vegetables
All vegetables except tomatoes and cucumber
  Some vegetable mixtures have artificial color or flavor - these are not allowed
Potatoes in any form

Main Protein Sources
Meats
  All meats not listed on elimination list
  All poultry
  All fish not flavored or colored

Legumes
  All dried peas, beans, peanuts except those colored or flavored
  All fresh eggs

Dairy Products
Milk
All natural cheeses
Plain yogurt
Vanilla and chocolate ice cream made with natural ingredients
Butter, not colored

Beverages
Homemade lemonade
7 UP
Coffee

Miscellaneous
Dry mustard
Jam, jellies made from permitted fruits, not artifically colored or flavored
Honey
Real mayonnaise
Distilled white vinegar
Homemade candies, without almonds
Homemade chocolate syrup - for all purposes

Instructions for Management with the M Diet (CONTROL Diet)

The diet lists all foods and products that are to be prohibited.

. Any item not on the list is permitted.
It is necessary to check every food package or container very carefully for chocolate or unenriched flour. In many cases, type of flour is not indicated. If the label does not read "enriched flour", do not use it. When in doubt, do not experiment - eliminate the food item.

3. With the difficulty in obtaining many food items on the market that conform to the allowed food list, it will be necessary to prepare many foods at home. Examples of this would be preparing food items that are normally sold prefried should be cooked a different way, and preparing chocolate containing foods only with instant chocolate.

4. The greatest success is usually observed when the entire family follows the diet. This removes the temptations from the child and facilitates compliance with the diet.

5. It is important that the child and family continue maintaining adequate nutrition during the study. For this reason, the foods on the allowed list have been grouped according to their contribution to the diet. A balanced diet which will maintain the nutritional status of the individuals following the diet can be achieved by choosing a certain number of foods from each group, to be eaten each day. The minimum number of servings from each group is suggested as follows:

Child	Adult
4 cereal and grains	4 cereal and grains
2 fruits (1 good source of vitamin C)	2 fruits (1 good source of vitamin C)
2 vegetables	2 vegetables
2 protein sources	2 protein sources
2 - 3 dairy products	2 dairy products

The foods listed under miscellaneous and beverages may be used as desired to complete the daily diet. This grouping of foods allows the child and family to choose a variety of food items which they like and will insure sound nutrition.

6. It is important to keep a diet diary for the days specified. This is the only method of control, as inadvertant infractions can be detected, and allows us to monitor the child's intake for nutrient adequacy.

7. You are asked to keep a daily record of infractions. We would hope that none occur. However, should infractions occur, it is important that you list all of them.

DIET M

PERMITTED food items

Cereal and Grain Products
Any cereal without artificial colors or flavors, dry or cooked
Any baked goods without artificial color or flavor - most baked goods will have to be prepared at home
All flours
All commercial breads except egg brand (usually dyed)

Fruits
Grapefruit*
Lemon*
Lime*
Pear
Pineapple
Banana
Juices of these fruits* without artificial flavor or color

*Good sources of vitamin C, juices may be labeled "vitamin C enriched"

Vegetables
All vegetables except tomatoes and cucumber
  Some vegetable mixtures have artificial color or flavor - these are not allowed
Potatoes in any form

Main Protein Sources
Meats
  All meats not listed on elimination list
  All poultry
  All fish not flavored or colored

Legumes
  All dried peas, beans, peanuts except those colored or flavored
  All fresh eggs

Dairy Products
Milk
All natural cheeses
Plain yogurt
Vanilla and chocolate ice cream made with natural ingredients
Butter, not colored

Beverages
Homemade lemonade
7 UP
Coffee

Miscellaneous
Dry mustard
Jam, jellies made from permitted fruits, not artifically colored or flavored
Honey
Real mayonnaise
Distilled white vinegar
Homemade candies, without almonds
Homemade chocolate syrup - for all purposes

DIET M

PERMITTED food items

Cereal and Grain Products

All cold cereal with milk and without chocolate
Converted or long-cooking rice
All bread products made with enriched white flour or whole wheat, c
Pastries without cream filling, made with enriched flour
Cakes and cookies without chocolate

Fruits

All fruits and their juices except those on elimination list
  oranges*
  strawberries*
* good sources of vitamin C

Vegetables

All vegetables not on elimination list
  (i.e., corn, beans, tomatoes**, brocolli**, carrots*)
**good sources of vitamins A and C
* good sources of vitamin A

Main Protein Sources

Meat
  Meats not on elimination list
  Luncheon meats, not containing by-products or ingredients
    on elimination list
  Chicken and turkey without skin
Legumes
  Dried peas and beans, lentils
  Baked beans without pork
Eggs - fresh or frozen but not fried

Dairy Products

Milk
Yellow cheeses and cheese food
Pudding, custards, ice cream not containing chocolate or
  unenriched flour

Miscellaneous

Pretzels
Cheese-corn snacks
Dessert toppings and syrups
Soup without noodles or eliminated vegetables
Baker's yeast
Wine and cider vinegar
Candy without chocolate
Margarine

Beverages
Cola drinks
Fruit flavored drinks without allowed fruits
Tea

Frequency

Name____________________

Subject Number________________

Condition____________________

Day____________

Week of________

		X/ Month									X/
1	Donuts	N	--	1	2	3	4	5	6	7	
2	Sugar coated cereals										
3	Oatmeal										
4	Home-made bread and rolls										
5	Store-bought bread and rolls										
6	"Natural" bread and rolls										
7	Graham crackers										
8	Store-bought cookies										
9	Chocolate cake										
10	Cake from a mix										
11	Macaroni, spagetti, noodles										
12	Oranges and orange juice										
13	Grapefruit and grapefruit juice										
14	Apples, juice and cider										
15	Bananas										
16	Tomato and tomato products										
17	Canned fruits										
18	Peas										
19	Green beans										
20	Corn and corn products										
21	Carrots										
22	Frozen vegetable combinations										
23	Potatoes										
24	Peanut butter										
25	Hamburger										
26	Pork or ham										
27	Luncheon meats										
28	Roasts										
29	Chicken										
30	Tuna fish										
31	Frozen fish sticks										
32	Butter										
33	Whole milk										
34	Chocolate milk										
35	Ice cream										
36	American cheese										
37	Cottage cheese										
38	TV dinners										
39	Margarine										
40	Sherbert										
41	Canned pudding										
42	Dinner helpers										
43	Home-made casseroles										
44	Canned soup										
45	Sandwiches										
46	Pancakes										
47	Plain dry cereal										
48	Soft drinks										
49	Chocolate candy										
50	Non chocolate snack food										

DIET RECORD

Name ____________________

Subject Number __________

Condition __________

Day __________

Week 1 2 3 4

Time	Place	Food	Description or Method of Prepare	Amount	Cod

Dietary Questionnaire

Name____________________ Age__________ Date____________

1. Usual meal times____________________

   (Sunday ____________________)

2. Between meal times a.m._________ p.m._________ b.b._________

   Usually what?____________________

3. Appetite: Good Varies Poor

4. Food dislikes____________________

   Will he try them?____________________

5. Food likes (10)____________________

6. Supplements - what and how often____________________

7. Problems at meal Table with child____________________

8. Meals at school (how and what)____________________

9. Any medical complications with food?____________________

10. Are there any changes in his food habits when the child is not on medication?____________________

Comments:____________________

LIST OF INFRACTIONS

Child's name ______________________
Diet assigned __________
Week of the __________

Date	Food item - description brand name	Amount	Why is this item considered an infraction	Behavior Observed

DIETARY DEGREE OF DIFFICULTY QUESTIONNAIRE

Scoring:

a = 0
b = 1
c = 2
d = 3
e = 4

Patient Name:______________________________
Patient Number:____________________________
Diet Code:_________________________________

1. How much extra shopping time was required to follow this diet?
    a. None
    b. Just a little
    c. Pretty much
    d. Very much

2. How much extra cost was required to follow this diet?
    a. None
    b. Just a little
    c. Pretty much
    d. Very much

3. How much extra time was required at home to prepare meals as a result of this diet?
    a. None
    b. Just a little
    c. Pretty much
    d. Very much

4. Compared to your child's "normal" diet, how much food was consumed during an average meal with this special diet?
    a. Much more
    b. A little more
    c. No difference
    d. A little less
    e. Much less

5. How many of your son/daughter's favorite foods were eliminated as a result of this diet?
    a. None
    b. Just a few
    c. A moderate number
    d. A large number

6. How often did your son/daughter complain about food items not available as a result of this diet?
    a. Not at all
    b. Just a little
    c. Pretty much
    d. Very much

7. On the average, how often did your son/daughter consume "forbidden" food items?
    a. 0 - 1 times per week
    b. 2 - 3 times per week
    c. 4 - 5 times per week
    d. over 5 times per week

8. In general, how difficult was it to comply with this diet?
   a. Not at all
   b. Just a little
   c. Pretty much
   d. Very much

9. Please note any other problems or difficulties you have had in following this diet.

____

____

____

____

____

These foods are to be ELIMINATED from diet

All fried foods - foods cooked in fat or oil (breaded or greasy foods)

Cereal and Grain Products
All hot (cooked) cereals (Maypo, oatmeal, farina)
Waffles
Pancakes
French toast
All crackers (Graham, saltines, cheese)
Corn bread
Instant rice
Cream filled pastries
Chocolate cakes and cookies
All foods containing unenriched white flour

Fruits
Grapefruit
Lemons
Melons
Bananas
Walnuts

Vegetables
Mushrooms
Lettuce
Peas
Panfried or french fried potatoes

Main Protein Sources
Meat
  Corned beef
Ham, pork, bacon
Fresh fish (frozen allowed)
Tuna fish
Chicken skin and turkey skin
Giblets

Legumes
  Peanuts
  Peanut butter

Dairy Products
Butter (margarine allowed)
White cheese
Chocolate pudding
Chocolate ice cream

Beverages
Rootbeer
Gingerale
Lemonade
Coffee
Chocolate milk

Diet M (con't)

Eliminated List

Miscellaneous
- Pickles in cloudy liquid
- Popcorn
- Chocolate syrup (instant chocolate, dry power is acceptable)
- Soup with noodles
- White sugar used at home
- Brewer's yeast
- Chocolate candy
- Distilled vinegar
- Honey

Sundry Items
- Chewing gum except for sugarless gum
- Deoderant soap
- Bubble bath
- Lemon shampoo
- Eye drops (except doctor's prescription)
- Egg-based paints
- Gummed envelopes, stamps, stickers, tapes

DIET STUDY FLOW SHEET

Revised Dec. 4, 1974

REFERRAL:

1. Basis of study explained
2. Referral information obtained
3. Informed that school information will be obtained - parents sent release of information forms to be signed and mailed back to WPIC
4. Informed that 24-hr recall will be obtained during first appointment
5. Appointment scheduled with coordinator in one week

6. Packet with letter to teacher and release of information form (signed) prepared and mailed:
    - a. Pretreatment: Teacher Questionnaire 000, Abbrev. Teacher Qs 013-
    - b. Baseline: Abbrev. Teacher Qs 053-083
    - c. Diet 1: Abbrev. Teacher Qs 093-113, Teacher Questionnaire
    - d. Diet 2: Abbrev. Teacher Qs 133-153, Teacher Questionnaire
7. Teacher contacted and her role is reviewed

FIRST APPOINTMENT:

1. Parents sign informed consent
2. Parent questionnaire obtained
3. Prior knowledge questionnaire obtained
4. Medical and social history obtained, IQ 85 verified
5. Allergy history obtained
6. Instructed to collect abbreviated parent questionnaires on each Tues and S for the next four weeks. If the child is on medication, it is to be discontinued on the first day of the thrid week. Parents called on the first day of the third week to remind them and answer any questions
7. Second appointment scheduled for one month (during fourth week)
8. Letter to physician mailed

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9. Instructed to collect diet diary on Mon, Tues, and Wed of week 1, and Thur Fri, and Sat of week 3. Phone call made on first day of thrid week
10. 24-hr recall and food frequency measure of past month obtained
11. Dietary questionnaire obtained

SECOND APPOINTMENT:

1. Physician performs psychiatric, neurologic and physical examination

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2. Instructed to collect abbreviated questionnaires on Each Sat for the next three weeks, and a Parent Questionnaire on the Sat of the fourth week
3. Diet assigned and requirements explained - instructed to collect diet diar on Mon, Tues, and Wed of week 1, and Thurs Fri and Sat of week 3. Parent called on the first day of the third week to remind her to collect diet diary and answer any questions. A list of infractions is to be kept throughout the period
4. Food frequency measure obtained for past month
5. Third appointment scheduled for one month (during fourth week)

6. Post card mailed to teacher to remind her that questionnaires need only be filled out on Fri's from now on

THIRD APPOINTMENT:

1. Instructed to collect abbreviated questionnaires and Parent Questionnaire (see above)
2. New diet assigned and requirements explained (see above)
3. Food frequency measure obtained for past month
4. List of infractions collected or verified
5. Dietary degree of difficulty questionnaire obtained
6. Fourth appointment scheduled in one month

7. Parents meet with Principal Investigator and fill our joint CGI

FOURTH APPOINTMENT:

1. Files checked to insure all data has been collected
2. Food frequency measure obtained for past month, list of infractions collected
3. Dietary degree of difficulty questionnaire obtained

4. Parents meet with Principal Investigator and fill out joint CGI
5. Parents are debriefed and interviewed to determine the amount of prior knowledge. Prior knowledge questionnaire obtained
6. Parents instructed on follow-up program for their child

7. Principal Investigator and coordinator complete discharge summary for each child.
8. Summary statement dictated and copies sent to physician, school, parent.

PARENT REPORTS

Medication Status During Pretreatment	Subject Number	Treatment Order															
		Pretreatment				Baseline				Control				K-P			
Medication	008	19	17	17	12	24	24	18	08	08	08	30	15	09	14	11	18
	010	17	15	19	14	18	20	21	21	18	18	18	23	18	18	16	15
	022	15	14	15	16	16	19	16	11	13	14	10	07	11	10	12	10
No Medication	527	11	10	08	13	16	15	05	13	11	11	16	18	05	05	05	06
	028	18	17	06	15	09	09	09	15	21	17	15	20	16	04	04	09
	030	12	12	13	14	09	18	10	17	02	07	08	09	04	05	08	07

PARENT REPORTS

Medication Status During Pretreatment	Subject Number	Treatment Order			
		Pretreatment	Baseline	K-P	Control
Medication	004	07 08 08 06	13 17 16 15	14 11 13 12 0	15 15 15 15 ↑
	006	10 15 13 14	17 25 16 17	06 08 05 07 ↓	09 08 07 14 ↓
	014	16 17 08 09	10 10 15 14	10 17 24 21 ↑	23 18 25 21 ↑
	021	10 11 10 08	15 16 07 11	11 06 06 06	19 14 12 14
	029	08 14 10 10	13 19 18 12	22 23 23 23 ↑	17 13 08 10 ↓
No Medication	001	25 28 28 22	27 23 27 25	24 18 18 18 ↓	20 26 29 27 ↑
	023	22 18 18 22	20 19 18 16	16 17 15 26 0 •	16 15 14 18 0 •
	533	18 18 19 18	21 16 16 16	23 16 18 25 0 ↑	17 14 11 17 ↓ 0
	036	23 14 12 13	19 15 17 15	15 09 25 29 0 ↑	16 14 15 25 0 ↑

TEACHER REPORTS

Medication Status During Pretreatment	Subject Number	Treatment Order															
		Pretreatment				Baseline				Control				K-P			
Medication	008	19	17	17	12	24	24	18	08	08	08	30	15	09	14	11	18
	010	19	18	17	13	19	18	16	18	10	10	18	18	09	12	12	12
	022	13	13	11	11	00	09	09	06	06	06	08	06	06	08	08	08
No Medication	527	14	19	13	06	17	18	15	15	19	15	18	16	07	12	09	14
	028	24	27	25	27	13	26	20	21	29	23	22	28	21	27	11	11
	030	27	27	27	17	27	27	23	14	15	08	24	15	09	17	01	11

TEACHER REPROTS

Medication Status During Pretreatment	Subject Number	Treatment Order															
		Pretreatment				Baseline				K-P				Control			
Medication	004	09	07	07	07	12	08	08	11 X	11	08	06	05	14	20	20	20
	006	03	00	00	03	03	03	02	00 X	00	01	06	00	00	00	00	00
	014	16	15	14	14	22	20	20	20	20	25	25	25 ↑	25	24	26	26
	021	22	16	14	21	24	27	30	26	15	19	23	29	22	19	29	29
	029	10	08	06	09	17	24	15	24	23	27	27	27 ↑	26	27	25	24
No Medication	001	21	19	13	13	13	13	17	21	16	13	09	09	11	13	15	15
	023	19	19	17	17	20	18	17	18	14	15	14	15	14	16	18	18
	533	08	08	08	08	03	04	06	04	10	08	05	08	09	10	12	12
	036	26	26	26	30	27	30	29	28	29	13	30	29	29	28	30	30

Patient no.	Feingold Diet	Control Diet
004	Lately he has been taking more interest in his school work -- he has proven to me that he is able to do the work. He just needs to work at it. He has been doing better but isn't always consistent. I do not consider him a behavior problem in the classroom.	
008	Some weeks his behavior improves and some weeks it appears to deteriorate. Overall, I have not noted any significant improvement in his behavior. At times I feel that his overall behavior may be a little bit worse.	Since the initial report, he has had one very good week and one very bad week. The other weeks have been the same or generally the same.
010	The biggest change has been his almost happy acceptance of warm gestures from me, such as an arm around his shoulder. Previously, he would recoil from a mere pat. While he still tends to deny responsibility for misbehavior, he is less shrill or excitable about it. All in all he seems to be a little more "put together".	
014	He has acted pretty much the same since he has been taken off the medication.	none
021	While he seems less to be groggy - or medicated - he is also less able to concentrate or use any controls to facilitate learning. He absolutely requires a one-on-one to get any sensible responses from him, though more often than not you get an irrelevant comment. Frequently he indicated he was really trying but the results were minimal.	There are no positive changes. If anything, he is demonstrating less rational behavior than before.

Patient no.	Feingold Diet	Control Diet
022	He seems to be an overly active child. He is doing more work in school than he was doing previously.	At times still fidgets, is overactive and disturbs the other children. However, he has improved in the above areas. I don't hear very many complaints about him from the other children. I only hear a few.
023	He has been somewhat more settled and has not been popping in and out of his seat as often as before. However, he has not been any quieter or more attentive.	He has been less fidgety and better able to sit in a chair than earlier in the year. He does not turn around as often and is somewhat more calm.
527	Less radical mood swings, less or shorter periods of depression, more consistent at "following directions" or working on a given task with less supervision.	Attention span much shorter; more frequent crying without apparent reason; aimless running.
028	Actually during this period his behavior became more erratic and at times worse than had previously been observed except during the aforementioned period of time. Academically, he continued to make progress as he has all year.	His behavior has not improved since my first report was filled out. He has his good and bad days. If anything, he has been having more consecutive bad days.
029	The pattern is much the same, except that behavior is worse. There is much more activity, much more evidence of frustration.	He still distracts children from work, even when he's involved in an art project. However, there is not so much interference with others at playtime. There is less withdrawing, more talking back. For a while he was fascinated with the words "penis" and "bum" and often drew pictures of these.

Patient no.	Feingold Diet	Control Diet
030	Physical reactions against other children have dropped almost completely. He is able to take correction without gross reactions. Picking up loose objects seems to have disappeared. He will give up objects when requested. Much calmer in class - more manageable in group - responds better to praise - seems interested in making friends.	His physical aggression has dropped. He rarely hits other children. Last 10 days prior to 5/8 seemed almost normal.
533	When given a punishment assignment, she appears very quiet, but will cooperate.	Seems more excitable.
036	He had one very good week the last of April, but with that exception he has been much more uncontrollable than when on medication. He has begun to steal from other children and hide what he takes.	At the previous report he would respond to behavior modification techniques being used, but he has lost touch with reality and only comes from his fantasy, would on occasion, to strike out violently. He rolls about on the floor and when an attempt is made to move him he bites, hits or punches.

Senator KENNEDY. The subcommittee stands adjourned.

[Whereupon, at 12:18 p.m., the subcommittee adjourned.]

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